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Nutritional Support and Hydration for Critically and Terminally Ill Elderly, by David A. Lipschitz and Ronni Chernoff, John L. McClellan Memorial Veterans Hospital, Little Rock, AK.

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Antibiotics and the Elderly, by David W. Bentley, William H. Barker, Kathryn M. Hunter, Peter D. Mott, Charles E. Phelps, and Patricia A. Tabloski, University of Rochester and Monroe Community Hospital, Rochester, NY.

Technology Assessment on Future Developments in Life-Sustaining Technologies for Elderly, by Yukihiko Nose, Makoto Usami, Takashi Horiushi, and Paul Malchesky, for the International Center for Artificial Organs and Transplantation, Cleveland Clinic Foundation, Cleveland, OH.

The Clinical Economics of Nutrition Support Services and Antibiotic Medications for the Critically and Terminally Ill Elderly, by Deborah S. Kitz, Henry Glick, and John M. Eisenberg, University of Pennsylvania, Philadelphia, PA.

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Nutritional Support and Hydration for Critically and Terminally Ill Elderly

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Assessment of the Nutritional Status in the Critically or Terminally Ill Elderly

Introduction

Malnutrition has been identified as a problem of increasing prevalence in hospitalized patients.[1-4] In addition, a greater incidence of nutritional deficiencies has been shown in institutionalized elderly; subclinical, subtle deficiencies have also been reported in ambulatory, apparently healthy, older individuals. In relation to the critically, terminally or chronically ill elderly, the most pressing issue is the detection, prevention and management of protein energy malnutrition. This section will primarily focus on this issue but will also summarize nutritional standards for apparently healthy, elderly individuals and delineate the potential impact of chronic diseases on the nutritional status of older hospitalized patients.

Standards of Malnutrition in the Elderly.

In order to develop a rational approach to the detection of malnutrition in the elderly it is important to examine currently available standards of normality. Nutritional status can be assessed using a variety of measures in a number of ways. Total dietary intake, as well as the proportion of intake from fat, carbohydrate and protein can be determined by 24 hr recalls and dietary histories. In addition, it is possible to determine caloric intake of subjects under close supervision by observation. Anthropometric measurements which evaluate total weight, muscle mass and fat stores are useful parameters of nutritional status. Finally, biochemical indices of visceral protein stores and hematologic measurements, as well as an assessment of vitamin and mineral status, should be taken into consideration in nutrition evaluation of older subjects.

A major problem with the standards for malnutrition in the elderly is the paucity of studies in apparently healthy, elderly adults of different ages. The most comprehensive survey of nutritional status of healthy Americans was obtained in the Ten-State Survey and the National Health and Nutrition Examination Survey (Hanes) which have been collected on two separate occasions from 1968 to 1970,[5] and from 1976 to 1980.[6] Most of the information reported here are derived from this data. It must be emphasized, however, that in many respects the results obtained in these populations cannot be extrapolated to standards for populations with different ethnic or socio-economic backgrounds. In the case of assessing nutritional risks in an ill elderly individual, standards encompassing hospital or institutionalized older people may be more appropriate. They are not, however, readily available.

Dietary Histories

There is good evidence that energy needs decrease with age, probably related to reductions in basal metabolic rates and to decreased physical activity. Thus average energy (or caloric) intake in elderly subjects is approximately one-third less than that of younger individuals. Interpretation of dietary histories in the elderly have been criticized because of issues of declining memory and senility. Recent studies,[7,8] however, have quite clearly documented that 24 hr dietary recalls and one week diet histories are relatively accurate in healthy older people who are living at home. Evidence was obtained that prospective one week diet histories are more preferrable than evaluation of retrospective short term 24 hr food consumption. In assessing diet histories, attention must be paid to subjects' economic status, food availability in the residence, physical capability to shop and cook, social contacts, personal esteem and level of appetite. Medication use (drug-nutrient interactions), nutrient supplementation and alcohol consumption should also be considered when determining variety and quantity of food usually consumed. In general, when obtaining a dietary history, nutrient intake should be compared to the results of major nutrition surveys and changes in usual patterans of specific individuals. The average dietary history results, in Hanes 2, for healthy elderly men and females are included in tables 1 and 2.

Anthropometric Data

Changes in weight, fat stores and lean body mass have been shown to occur with advancing age.[9] Lean body mass decreases resulting in an increase in the proportion of body weight as fat. In addition, a redistribution of fat stores occur, particularly in females, with an increase in the proportion of fat around visceral organs. The interpretation of anthropometric measurements is aggravated by the fact that ageing is associated with a reduction in height, which is commonly employed as a reference measure in these studies. The changes which occur in height, averaging 2.9 cm loss in men, and 4.9 cm loss in women, make its use as a reference standard somewhat difficult. Accurate heights are also difficult to determine in some older adults, especially if they are bedfast or confined to a wheelchair. Recently we have suggested the use of total arm length as a more appropriate measure of stature in developing anthropometric standards for the elderly.[10] Others have suggested the use of knee to ankle measurements.[11] Although having advantages over height these measurements are still not perfect as they do not factor in whether or not individuals have large, medium or small frames. It is clear, however, that assessment of stature is one of the most important research issues requiring attention in nutritional assessment of the elderly. The changes in height that occur with age, as well as difficulties with skinfold thickness parameters, make the interpretation of anthropometric measurements in the elderly extremely difficult.

Of particular concern is the lack of appropriate standards for weight in the elderly. Even in large epidemiologic surveys[12] the development of accurate measures of ideal body weight (for height) are not readily available. The best weight for height chart information that has been developed is that described by Masters.[13] However, it was developed from a relatively small population of older Americans and does not reflect the broad diversity of our population. The average weight in pounds per inch in height in persons age 65-94 for men and women, described by Master is shown in tables 3 and 4.

The value of skinfold measurements in assessing the nutritional status of individual older persons is marginal at best. However, from a survey standpoint, skinfold measurements do support the finding that body fat increases with advancing age. Studies have demonstrated that alterations in fat distribution, altered skin turgor and elasticity and other characteristic changes of the aging skin make skinfold measurements difficult to interpret after age 60. There is evidence that subscapular skinfold measurement is a more reliable measure of fat stores in men and that extremity measurements are more reliable in women. It is generally accepted that more than one skinfold measurement should be determined to increase the validity of the measurements (Tables 5 and 6). However, multiple measurements are frequently impracticable. Tricep skinfold values, derived from several different studies, yield remarkably similar mean values suggesting, at least, reproducibility. The data developed by Frisancho[14] for tricep skinfold thickness constitute the best available standard information for these measurements. Other data describing standards for subscapular skinfold thickness or truncal thickness, are still too limited to be described.

The tricep skinfold is used to estimate body composition, and, with the concomitant measure of midarm circumference, can be used to calculate midarm muscle circumference and midarm muscle area. Studies have confirmed the ability of midarm muscle area to predict lean body mass and formulas have been developed that allow the calculation of corrected arm muscle area for adults.[15,16] Although standards for midarm muscle area have been reported for elderly subjects[14] the results leave much to be desired. The study is also limited by the fact that the oldest subject examined was age 75 (Table 7).

Creatinine Excretion as a Measure of Lean Body Mass

Twenty-four hour excretion of urinary creatinine varies directly with muscle mass of the body with reasonable accuracy. This measurement, related to height, has been used as an assessment of lean body mass in the diagnosis of nutritional deficiencies in hospitalized patients. The creatinine height index, however, developed by Bistrian et al,[17] used an extremely small population of young adults to develop normal values. At the current time there are no standards for creatinine excretion for the elderly and its use in the assessment of nutritional status of older subjects is very limited and may be affected by age-related changes in renal function.

Biochemical Measurements

Serum albumin is the most frequently used biochemical index of nutritional status, although many factors dramatically alter the serum concentration. The protein functions as an acute phase reactant and decreases in the presence of acute or chronic disease. Marked reductions in serum albumin also occur in the presence of liver disease or excessive urinary or gastrointestinal loss of protein. Most surveys show that the range of serum albumin concentrations in the elderly are broader than that found in the young; but the majority still fall within the normal range. The mean value of serum albumin declines perceptibly with age and, although synthesized at normal rates, the serum albumin is less responsive to dietary protein refeeding. Significant reductions of serum albumin concentrations outside the lower limits of normal is rare in healthy elderly. For this reason the presence of hypoalbuminemia (serum albumin < 3.5 gm/dl), in the absence of liver disease or excessive losses of protein from the body provides strong evidence of nutritional deprivation.

Serum transferrin is a a frequently used index of visceral protein status. However, there are several difficulties with interpretation of the measurement. Iron deficiency anemia increases the transferrin concentration while the anemia of infection and inflammatory diseases decreases the level. Transferrin levels also vary inversely with tissue iron stores. Since iron stores are higher in the elderly than in younger subjects their transferrin levels are lower. Thus, many apparently healthy elderly subjects, have serum trfansferrin levels in the range usually described as deficient, not because of nutritional deficiencies but because of an increase in tissue iron stores. For this reason hypotransferrinemia must be interpreted with caution.

Both pre-albumin and retinol binding protein have been suggested as rapidly responsive protein status indices, but the use of these measurements has been primarily in ill people and rarely in the elderly. Further work will be required to determine the importance of these measurements in detecting nutritional deficiencies in older people.

Hematologic Measurements

A higher prevalence of subjects with hemoglobin levels below the generally accepted normal range has been extensively reported in healthy elderly individuals. This difference is particularly obvious when elderly male subjects are examined. The decrease in hemoglobin that occurs with aging is generally not due to the commonly recognized causes of anemia such as iron deficiency, the anemia of chronic disease or folate deficiency. Elderly subjects have been shown to have an overall reduction in hematopoiesis.[18] It is not clear at this stage whether this decrease in hematopoiesis reflects the normal aging process or some yet to be defined abnormality. This is the probable mechanism for the lower hemoglobin levels in apparently healthy elderly subjects. For this reason the presence of an apparent mild anemia may not indicate pathology. If, however, the anemia is more severe (hemoglobins < 10 gm/dl for females or < 12 gm/dl for males) a hematologic or nutritional abnormality should be strongly suspected. Anemia is invariable in elderly subjects with protein energy malnutrition.

Immunologic Assessment

Differences existing in the immune response of young and elderly subjects are clear cut and dramatic. Thymic involution accounts for the major age related change in the immune system.[19] This involution results in a loss of the capacity of the thymus to differentiate T cells from lymphoid cells of earlier lineage (pre-T cells).[20] Although the total number of T lymphocytes does not change with age the proportion of T cell sub-populations is altered. The number of immature T cells in the blood is higher in the elderly. There is a relative increase in the number of T suppressor cells and a reduction of T helper lymphoid cell number. An alteration in the distribution of T cells is thought to account for the increased prevalence of auto-antibodies and incidence of benign monoclonal gammopathies that accompany aging.[21]

A reduction in cell mediated immunity is the most obvious feature of the senescent immune system. Fifty percent of healthy persons over the age 50 have impaired delay cutaneous hypersensitivity.[22] Furthermore the lymphocytes from aging humans have a reduced ability to undergo blastogenic mitosis when exposed to mitogens. Lymphocytes from the elderly proliferate less when activated than do lymphocytes from young subjects.[23] Recent observations suggest that this response is primarily due to the loss of thymic influence. When T cells from elderly subjects are exposed to thymic hormone they regain their immuno-competence.[22]

Changes in humoral immunity (B cell function) with aging are more subtle. Studies on the effect of age on antibody production have yielded conflicting results; perhaps due to the wide range of experimental values generally observed in elderly individuals. It has, however, been well established that aging is significantly associated with the presence of various auto-antibodies, in particular antibodies against nuclear antigens.[21] There is also evidence that aging affects the rate of antibody production by activated B cells.[23]

Protein energy malnutrition and an array of single nutrient deficiencies causes changes in immune function which are virtually identical to those which occur as a result of the aging process. Thus protein energy malnutrition causes anergy, decreased cell mediated immunity, changes in T-cell function identical to those of aging and subtle alterations in B-cell humoral activity. Lymphocytopenia, frequently described as a result of normal aging, also occurs in protein energy malnutrition and other single nutrient deficiencies. For this reason the use of immunologic parameters as an index of nutritional status in the elderly must be interpreted with caution. It must be emphasized, however, that protein energy malnutrition aggravates the immunologic changes that occur with normal aging and that improvements in immune function with nutritional repletion have been reported (see below).

Vitamin Status

There are several vitamins for which the elderly may be at particular risk for deficiency and others for which most national studies indicate little risk. Dietary studies have shown that significant numbers of healthy elderly subjects have decreased dietary intake of the B vitamins, particularly thiamine and riboflavin.[7] Studies using urinary and functional tests of B vitamin status confirm the frequency of these deficiencies.

Few studies have examined folate and B_{12} status in the elderly. Most have demonstrated that although the values for these vitamins appear to decrease with age, deficiencies of any severity are quite rare.[24]

Earlier surveys of vitamin intake in the elderly showed widespread vitamin C deficiency. More recent studies, however, have found that vitamin C intake is adequate in the elderly and that deficient serum and cellular levels of the vitamin are uncommon.[25]

A recent assessment of vitamin A status in the elderly indicates an excellent intake which was similar to the intake found in younger subjects. No evidence of significant vitamin A deficiency was detected for all age groups.[7] Masud, Baker and others[26,27] have expressed concern over the active vitamin D content of the elderly and have suggested that plasma 25 hydroxy vitamin D concentrations/decreases due to poor dietary intake and lack of sunlight and exposure. This, coupled with a decreased calcium intake and lack of exercise may contribute substantially to the osteoporosis that is so prevalent in the elderly.

Calcium Mineral Status

It is clear from the high prevalence of osteoporosis in the elderly that total body calcium levels decline with aging.[28] Most studies, however, demonstrate that age related bone loss is of multifactorial origin. There is evidence suggesting an increase in the requirement for dietary calcium with age. This increase in calcium requirement is primarily related to a reduction in the absorptive capacity of the gastrointestinal tract. For this reason levels of dietary calcium intake, sufficient to offset obligatory calcium losses in young adulthood may be insufficient for the elderly. Excessive amounts of dietary phosphorous or protein may also contribute to bone loss although their contribution is less clear. There is also evidence that in selected elderly persons, vitamin D deficiency may be an added risk factor. These observations must be taken into account when assessing the calcium needs of older individuals. Most dietary recall studies indicate either normal to low calcium intakes in the elderly. Dietary data from Hanes II confirm that calcium is the highest risk nutrient for inadequate intake.[7]

Zinc

Surveys of the elderly have generally not found reduced levels of copper and zinc, although this data is controversial. Although zinc deficiency is hard to identify, the similarity between the immune and hematopoietic changes which occur as a result of aging and those which occur as a result of protein energy malnutrition and zinc deficiency make attention to this nutrient a critical area when assessing nutritional status of the elderly.

Impact of Chronic Diseases on the Nutritional Status of the Elderly

It must be emphasized that the chronically or terminally ill elderly invariably have major or multiple diseases that predispose to or aggravate nutritional deficiencies. The average number of major diseases requiring medical attention in frail older subjects assessed in geriatric evaluation units is 7.5 and in patients admitted to nursing homes it is 8. These diseases which include infections (acute and chronic), neoplasia, cerebrovascular and cardiovascular disorders, chronic renal, pulmonary, hepatic or cardiac failure, all affect nutritional status through multiple mechanisms. Decreased nutrient intake is extremely common because of anorexia caused by the disease itself. Anorexia is compounded by the development of deficiencies in nutrients which affect appetite and taste (vtamin A and zinc). Altered gastrointesinal absorptive capacity as a result of age and disease is compounded by protein depletion, which itself affects mucosal cell proliferative capacity. This in turn results in a vicious cycle of worsening nutrition, decreased nutrient absorption and aggravation of anorexia. Disease also results in increased requirements for nutrients. Energy and protein needs increased twofold or more in the presence of moderate stress. If the stress is not accompanied by appropriate intakes of energy and protein, malnutrition develops rapidly. Although not proven it is extremely likely that nutritional reserve capcity is decreased in the elderly and as a result they are more susceptible to problems when intake is compromised. Finally disease and nutritional deficiency compound the age related diminution in host defense. Immunological and granulocyte function as well as hepatic detoxifying mechanisms are markedly diminished in the malnourished older person. Thus these subjects are more susceptible to infection which leads to a much higher morbidity and mortality.

From the above discussion it is clear that nutritional deficiences are likely to be very common in the elderly with chronic disease. Because of similarity between the effects of age and nutrition on multiple cellular and physiologic functions, there is a good chance that a potentially correctable nutritional deficiency may be overlooked or ascribed to normal aging. It is this fact which makes the paying of attention to nutritional factors so important.

Nutrition, Drugs and the Elderly

Because of the presence of multiple diseases as well as non-specific complaints, the elderly can take large numbers of drugs which can have major impact on nutritional status. Conversely the aging process and nutritional status markedly affect and alter drug metabolism. Thus a complex age- nutrient-drug interaction exists in these subjects and this fact must be taken into account when evaluating the nutritional status of chronically or terminally ill elderly.[29] Various nutritional factors alter the absorption, distribution, metabolism and excretion of drugs. Macronutrients, such as carbohydrates, proteins and fats, as well as trace substances such as vitamins and minerals, are often responsible. Nutrient components can change gastrointestinal motility, secretions involved in the digestive processes, blood flow rates and enzyme activity responsible for drug metabolism. Evidence is strong that foods and nutrition can be a major determinant of drug action.

Conversely, numerous drugs can interfere with nutrient metabolism. Examples of these changes are listed in table 8.[30] The table summarizes the wide array of nutrient changes which can occur in nutritional status when drugs are used in the elderly. The mood altering drugs must be specially mentioned. Alteration in cognitive function and mental status can markedly affect the quality and quantity of food consumed and both potentiate and aggravate nutritional deficiencies.

Protein Calorie Malnutrition

The prevalence of protein calorie malnutrition (PCM) in hospitalized patients has been reported in the literature, as previously described. The true incidence of this disorder among subjects beyond the age of 65 remains in question. The elderly do constitute the majority of hospitalized patients, and it is our experience that the highest prevalence of malnutrition occurs in this group. The disorder is frequently overlooked or completely ignored while attention is focused on the primary reason for hospitalization. This section describes the clinical features of PCM in the elderly and problems with its diagnosis. The importance of malnutrition in the aged cannot be overemphasized because of the relative ease with which nutritional abnormalities can be corrected.

Etiology and Significance

As in any other age group PCM in the hospitalized elderly patient is usually secondary to a primary disease that required hospitalization. The major mechanism resulting in PCM is poor nutrient intake due to central anorexia. The best described example of PCM is the cachexia that occurs in patients with cancer.[31] In addition, PCM can occur in the presence of chronic heart failure, chronic lung disease, renal failure, hepatic disease, and other chronic problems. Finally, economic factors, severe depression, decreased ability to cook meals, loneliness, and isolation can all severely compromise the diet of indigent elderly.

It is critical to recognize PCM because of the major effect that it has on the ability of the malnourished individual to respond to stress, heal wounds, or fight infections. An adequate nutrient supply is particularly essential for organ systems with rapid cellular turnover (skin, gastrointestinal tract, bone marrow) and those with large protein turnover (liver). Thus, flaky paint dermatitis, malabsorption and depressed serum protein levels are frequently the results of poor nutrient intake.

Clinical Presentation

The clinical features of PCM in the aged are relatively uniform. Three broad groups of patients can be identified. The largest group consists of those patients admitted to hospital with a primary disease. Secondary PCM may be present on admission or alternatively may develop during the course of a complicated hospital stay. A second, smaller group, includes patients with primary PCM who present to the hospital with an acute infection probably resulting from the nutritional deficiency. They are usually over the age of 70 years, indigent, and have marginal social circumstances. Either no history is available or a responsible family member indicates that over the past few weeks an obvious change in the mental status of the patient had occurred. When a dietary history is available, it usually indicates grossly inadequate intake and frequently there is a history of being unable or unwilling to cook. Recent loss of a spouse is common, and severe endogenous depression should be suspected. A final group presenting to hospital with PCM are institutionalized patients. Often prolonged tube feeding has been required because of a previous cerebrovascular accident or other severe organic brain syndrome. Poor nutrient intake is particularly common in elderly subjects who have recently been institutionalized.

The most frequent symptom of PCM in the elderly is confusion or a history of recent alteration in mental status. This may be present on admission or a change in mental status may be noted in the hospitalized patient. The symptom is extremely nonspecific in the elderly and is frequently the initial manifestation of heart failure, infections, metabolic disturbances, or acute cerebrovascular event. Recent studies have shown that dehydration is the single most common cause of an acute confusional state in the elderly.[32] In patients with PCM, inadequate fluid intake is often present so that the etiology of confusion probably relates to dehydration. In patients who have been hospitalized for some time, a careful examination of the record usually reveals a significant weight loss from the time of admission. This is particularly common in aged subjects recovering from recent major surgical procedures. In the past, we have evaluated 15 such patients for the presence of PCM.[33] Of these, the majority (11 patients) required emergency surgery including aneurysm repair, appendectomy, and a variety of orthopedic procedures. Their initial postoperative course was usually uneventful, but after a period ranging from 14 to 30 days the patients became more and more confused and increasingly bedfast. A review of their hospital charts revealed a weight loss which ranged from 6 to 15 per cent of their original weight at admission. In 12 of the 15 an acute infection unrelated to the surgical procedure developed and in two wound sepsis occurred. Infections included pneumonia and urinary infections, and in one patient septicemia of unknown cause was found. Physical examination occasionally reveals a clue to the presence of malnutrition. Flaky paint dermatitis may be seen, and glossitis is common. The obvious manifestations of kwashiorkor (protein malnutrition) or marasmus (protein calorie malnutrition are unusual). In some patients dehydration may be obvious, but in others edema is present.

Diagnosis

The single parameter of nutritional assessment affected the least by the aging process is serum albumin. Irrespective of age or sex, it is extremely unusual to find a healthy subject with a serum albumin value less than 4 gm per dl. In contrast, a value greater than 3.5 gm per dl is extremely unusual in aged subjects with PCM. It must be emphasized that many factors affect measurements of serum albumin. The protein behaves as an acute phase reactant with modest reductions occurring in a wide variety of acute disease processes. In addition, prior to ascribing hypoalbuminemia to PCM, hepatic dysfunction and renal or gastrointestinal losses of protein must be excluded. As described above there are serious limitations for the use of anthropometric measurements, serum transferrin, hematologic or immunologic parameters in the assessment of the nutritional status of the elderly.

Based upon the above discussion and in the absence of suitable standards for the elderly the following criteria for diagnosing PCM are recommended: 1) a careful history and physical examination will often provide strong clues to the presence of PCM; 2) a history of recent weight loss together with a serum albumin less than 3.5 gm dl not due to hepatic failure or renal losses of protein is the most important diagnostic finding; 3) anemia, lymphocytopenia and anergy are invariably present and support the diagnosis; 4) Other anthropometric measurements, and evaluation of lean body mass are currently of little value in diagnosis of PCM in the aged.

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Table I

Reported Intakes of Individuals Over 65 in the U.S. Population
Data from NHANES II 1976 - 1980 FEMALES

Nutrient	Mean Intake	+		Percentile Distribution (compressed)				
	Stand. Err.	Mean	RDA	5	25	50	75	95
Calories	1295	17	1600	607	972	1221	1570	2172
Protein(g)	51	.7	44	21	36	48	63	92
Carbohydrate(g)	158	3.1		64	111	151	194	284
Fat(g)	50	1.0		16	33	46	62	99
Calcium(mg)	542	11	800	141	298	475	714	1156
Phosphorus(mg)	854	13	800	344	585	809	1051	1539
Iron(mg)	10.22	.18	10	4.28	6.63	9.05	12.20	19.81
Sodium(mg)	1990	38		678	1269	1812	2425	3891
Potassium (mg)	1965	31		807	1367	1857	2450	3429
Vitamin A(iu)	5481	249	5000	832	1987	3346	6225	15500
Niacin(mg)	14.42	.29	13	5.19	8.96	12.90	17.35	30.09
Thiamine(mg)	.99	.02	1.0	.37	.63	.85	1.15	1.96
Riboflavin(mg)	1.36	.04	1.2	.42	.79	1.13	1.60	2.88
Vitamin C(mg)	105	2.9	60	7	37	90	147	260

Values usually rounded to the nearest tenth. Abstracted from Dietary Resource Data DHHS Pub. No. (PHS) 83-1681, 1983.

Table 2

Reported Intakes of Individuals Over 65 in the U.S. Population
Data from NHANES II 1976 - 1980 MALES

	Mean Intake +			Percentile Distribution (compressed)				
Nutrient	Stand. Err.	Mean	RDA	5	25	50	75	95
Calories	1829	24	2000	841	1335	1723	2212	3096
Protein(g)	73	1.0	56	29	51	67	90	135
Carbohydrate(g)	204	3.3		72	141	193	253	366
Fat(g)	75	1.2		27	49	68	93	141
Calcium(mg)	698	13	800	186	370	597	915	1564
Phosphorus(mg)	1186	15	800	483	812	1112	1447	2244
Iron(mg)	14.10	.24	10	5.49	9.13	12.31	17.05	27.92
Sodium(mg)	2894	49		1047	1844	2583	3596	5603
Potassium (mg)	2393	34		863	1605	2261	2985	4336
Vitamin A(iu)	6577	364	5000	976	2236	3929	7077	17161
Niacin(mg)	19.95	.33	16	6.56	12.48	17.68	24.14	40.24
Thiamine(mg)	1.33	.03	1.2	.47	.82	1.13	1.57	2.77
Riboflavin(mg)	1.84	.04	1.4	.57	1.07	1.56	2.25	3.95
Vitamin C(mg)	100	3.5	60	5	33	79	140	271

Values usually rounded to the nearest tenth. Abstracted from Dietary Resource Data DHHS Pub. No. (PHS) 83-1681, 1983.

Table 3

Average Weight in Pounds per Inch of Height in Persons Aged 65-94

MEN

	Age in Years					
Height In.	**65-69**	**70-74**	**75-79**	**80-84**	**85-90**	**90-94**
61	142	139	137	—	—	—
62	144	141	139	135	—	—
63	146	143	141	136	133	—
64	149	146	143	138	135	—
65	151	149	145	141	139	130
66	154	152	148	144	142	133
67	156	155	151	147	145	136
68	158	158	154	150	148	140
69	163	162	158	154	152	144
70	167	165	162	159	156	149
71	172	169	166	164	160	154
72	177	173	171	170	165	—
73	182	178	175	—	—	—

Adapted from Master (12)

TABLE 4

Average Weight in Pounds per Inch of Height in Persons Aged 65-94.

WOMEN

Age in Years

Height In.	65 69	70-74	75-79	80-84	84-89	90-94
58	133	125	123	-	-	-
59	134	127	124	116	110	-
60	135	129	126	118	113	-
61	137	131	128	121	116	-
62	139	134	131	124	120	119
63	141	137	134	128	124	119
64	144	140	137	132	128	120
65	147	144	140	136	133	124
66	151	147	143	140	138	129
67	155	151	146	144	142	-
68	159	155	-	-	-	-
69	164	160	-	-	-	-

Adapted from Masters

Table 5

Sex-Specific Reference Values
for the Subscapular Skinfold Thickness
for Americans over Age Fifty-Five*

HANES I

Age Group Years	Percentile 5	10	25	50	75	90	95
				MEN			
55-64	6.0	7.0	11.0	15.5	21.0	27.0	30.0
65-74	6.0	7.5	10.5	15.0	20.0	25.0	30.0
				WOMEN			
55-64	7.0	8.0	12.5	20.0	28.0	34.5	38.0
65-74	7.0	8.0	12.0	18.0	25.0	32.5	37.0

*Developed from data collected by HANES I
Abstracted from Grant, J.A. et al. (16)

Table 6

Subscapular Skinfold Percentiles for Men and Women over 55

Tecumseh, Michigan

AGE	(Values in mm) MALE SUBJECTS			(Values in mm) FEMALE SUBJECTS		
	Percentiles			Percentiles		
	20	50	80	20	50	80
55-59	11.8	18.8	30.7	13.5	22.3	32.0
60-64	9.3	16.8	24.8	15.5	22.4	33.6
65-69	8.0	12.5	17.4	13.0	20.9	30.0
70-74	8.7	14.3	23.1	14.0	22.6	29.9
75-79	9.9	14.8	20.8	10.0	21.6	31.2
80+	7.4	9.3	23.4	8.2	14.0	23.0

Adapted from Montoye, H.J. et al. (14)

Table 7

Percentiles for Upper Arm Anthropometric Data for Whites over 55 in The United States

Health and Nutrition Examination Survey I
1971 to 1974

Age Group	Percentiles						
	5	10	25	50	75	90	95
Males	**Triceps Skinfold (mm^2)**						
55-64.9	5	6	8	11	14	19	22
65-74.9	4	6	8	11	15	19	22
Females	**(mm^2)**						
55-64.9	12	16	20	25	31	36	38
65-74.9	12	14	18	24	29	34	36
Males	**Arm Muscle Circumference (mm)**						
55-64.9	236	245	260	278	295	310	320
65-74.9	223	235	251	268	284	298	306
Females	**(mm)**						
55-64.9	187	196	209	225	244	266	280
65-74.9	185	195	208	225	244	264	279

Adapted from Frisancho (14)

TABLE 8

DRUG INTERFERENCES WITH NUTRITIONAL STATUS

Drugs	Mechanism	Effects
Anthistamines	Appetite stimulation	Weight gain
Antihypertensives (ganglionic blockers)	GI motility effects	Generalized malabsorption
Antiinfectives		
Aminoglycosides	Enzyme inactivation	Reduced carbohydrate metabolism
Chloramphenicol	Impaired nutrient metabolism and utilization	Protein-binding inhibition
Isoniazid	Altered nutrient excretion	Pyridoxine deficiency
Neomycin	Bile acid activity interference	Reduced vitamin B_{12}, carotene, iron, sugar, triglyceride absorption
Trimethoprim	Impaired nutrient metabolism and utilization	Folate deficiency
Antineoplastics		
Aminopterin	Damage to intestinal mucosa	Reduced vitamin B_{12}, carotene, cholesterol, lactose, D-xylose absorption; megaloblastic anemia, steatorrhea
Methotrexate	Damage to intestinal mucosa; impaired nutrient absorption	Same as above; decreased folic acid synthesis
Antirheumatoids (colchicine)	Damage to intestinal mucosa	Same as above
Central-nervous-system drugs		
Amphetamines	Appetite suppression	Weight loss
Benzodiazepines	Appetite stimulation	Weight gain
Levodopa	Competition for uptake at blood-brain barrier	Reduced phenylalanine and tyrosine absorption
Phenobarbital	Impaired nutrient metabolism and utilization	Vitamin D deficiency
Phenothiazines	Appetite stimulation	Weight gain
Phenytoin	Impaired nutrient metabolism and utilization	Osteomalacia
Tricyclic antidepressants	Appetite stimulation	Weight gain
Gastrointestinal drugs		
Aluminum hydroxide gel	Complex formation with nutrients	Reduced phosphate absorption
Antacids	Altered GI pH	Thiamine deficiency
Anticholinergics	GI motility effects	Generalized malabsorption
Cathartics	GI motility effects	Calcium and Phosphorus loss
Cholestyramine	Bile acid activity interference	Vitamin A, D, E, and K deficiencies
Clofibrate	Enzyme inactivation	Reduced carbohydrate absorption
	Appetite suppression	Weight loss
	Bile acid activity	Reduced vitamin B_{12}, carotene, iron, sugar, triglyceride absorption
Immunosuppressives		
Cytotoxic agents	Appetite suppression	Weight loss
Steroids	Altered nutrient excretion	Sodium depletion in adrenally suppressed patients

Adapted from Lamy PP *Clin Nutr* 2:9, 1983.

PART 2

INTRODUCTION

The use of enteral and parenteral nutrition has increased dramatically during the past decade. As a reflection of utilization, the market for enteral and parenteral nutrition solutions and administration devices . has grown explosively. According to Adult Enteral/Parenteral Nutrition Markets in the U.S., Frost and Sullivan, Inc., (April, 1985), the total market was over $535 million in sales in 1983, approximately 55% of the sales in parenteral products and 45% in enteral products. The primary purchasers are hospitals, nursing homes and home health care. Of these purchases, hospitals account for 68.5% of the market, nursing homes account for 11% and the remainder is in home use. According to Frost and Sullivan, nursing homes are approximately 5 years behind hospitals in utilization and purchasing trends. The home market has shown significant growth rates in the use of parenteral nutrition; however, enteral sales have been affected by unfavorable reimbursement policies from federal and state governments. The guidelines established for the reimbursement of these services for medicare patients has been a factor in utilization.

Based on the present guidelines, nutritional therapies are reimbursed if they are replacing, on a permanent basis, a dysfunctional gastrointestinal tract. Malnutrition, or other transient conditions are not covered unless they are caused by permanent impairment of an organ. Enteral formulas administered with or without a tube, are not covered unless they meet the permanency guidelines. Since the bulk of the enteral market (approximately 3/4 of all sales) is in general purpose as opposed to disease-specific or specialized formulas, it can be assumed that a large portion of enteral feeding usage is not reimbursable. Ironically, the reimbursement guidelines encourage use of parenteral nutrition support for home care, which is more expensive and potentially more dangerous.

A market analysis indicates a strong growth in the use of nutritional products by middle-aged and elderly persons who are the most rapidly increasing segment of the population.

To best address the tasks defined in the contract, information regarding delivery of products and services provided to the patient directly had to be collected. To most efficiently gather this information, a mail survey was conducted on all members of the American Society for Parenteral and Enteral Nutrition residing in the continental United States. These individuals were chosen as the most knowledgeable due to their direct patient care responsibility. Approximately 4,000 questionnaires were sent to A.S.P.E.N. members and 469 completed questionnaires were returned. An additional 75 questionnaires were returned with notes attached about the inappropriateness of the questionnaire for their patient population, primarily pediatrics. Although this may not seem like a high rate of return, most institutions that have nutrition support services have more than one A.S.P.E.N. member. In many instances it was indicated that the individual completing the questionnaire was responding for the entire team. Therefore, it can be speculated that approximately three or four A.S.P.E.N. members per institution were surveyed. If one analyzes the data considering that approximately 1200 institutions were surveyed, the return rate was approximately 45%.

The respondents included 64 surgeons, 48 internists, 76 registered nurses, 193 registered dietitians, 83 registered pharmacists and others identified as doctors of osteopathy, doctors of philosophy or respiratory therapists. The characteristics of the responses are shown in Table 1 and 2. Sixty-five percent work in institutions of 250 - 499 or 500 - 1,000 beds (see Table 2). These can best be characterized as critical care, private, community institutions. Approximately 25% of the hospitals included are University-affiliated (see Table 3). Nutritional support services in these institutions have been functioning for a number of years. Only 24 nutrition support services have been in existence under one year. One hundred thirty-eight services have been in existence from one to three years and 165 services have been functioning from four to six years. Only 81 of the respondents indicated their nutrition support services had been in existence from 7 to 10 years. This was an arbitrarily assigned cut-off point, since the development of nutrition support services can be closely paralleled with the establishment of the American Society for Parenteral and Enteral Nutrition in 1976.

Sample Biases

It must be noted again that the sample population are health care practitioners who are presently members of A.S.P.E.N. Because these individuals are actively engaged in the provision of parenteral and/or enteral nutrition to patients in the hospital or at home, they have a bias towards the use of these technologies. Many of the questionnaires were completed jointly by more than one team member. It is likely, although not confirmed, that the attitudes reflected by this survey are common among professionals participating in this type of medical support. Most of the attitude items were clearly biased in one direction, indicating consistency among the respondents who completed the survey.

It is difficult to determine whether health care practitioners who are involved in nutrition support and are not A.S.P.E.N. members have similar attitudes. However, it is reasonable to expect that, since involvement in nutrition support is usually voluntary, attitudes of non-A.S.P.E.N. member practitioners involved in nutrition support are similar to those documented by this survey.

Health care practitioners who are not involved in nutrition support can not be assumed to have the same views as clinicians who are actively involved in nutrition support. Based on the relatively small number of identified nutrition support services (estimated 600-900) for approximately 6500 hospitals in the United States, it can be concluded that there has not been a general acceptance of nutrition support teams.

Approximately 4000 A.S.P.E.N. members comprise the 600-900 nutrition support services. The range is very broad due to several factors. No one seems to be able to compile a complete list despite periodic attempts to do so by Ross Laboratories, Nutrition Support Services Magazine and A.S.P.E.N. One explanation may be the intermittent dissolution of these teams as a cost-cutting measure by hospital administrators. Based on the approximation of 6500 U.S. hospitals of 50 beds or more, the percent of hospitals with nutrition support teams is between 9-14%.

Survey Results

The results of the survey indicate that an average of 38 patients per month per respondent receive enteral feeding and of these 50% are over aged 65. An average of 22 patients per month per respondent receive parenteral feeding. Of these 39% were over aged 65. Considering that 780,300 patients in U.S. hospitals received enteral nutrition in 1984 and 536,200 received parenteral nutrition, the scope of use of these therapies in individuals over age 65 is enormous, approximating 600,000 patients per year. Most respondents seemed to keep reasonably accurate records on the numbers and ages of their patients. However, on questionnaire items that asked about costs for parenteral and enteral nutrition, approximately one-third of the respondents were unable to provide this information. The mean cost per liter of enteral formula is $9.70 (range: $1.10 - $42.00). The mean cost per patient per day, including solutions, equipment, supplies and personnel time is $42.88 (range: $4 - $132). The mean cost per liter of solution for parenteral support is $71.00 (range: $10 - $250); and the total cost, including solutions, equipment, supplies and personnel for parenteral support is $196.00 (range: $25 - $500) per day (Table 4). Patients receiving enteral feedings have a mean length of hospital stay of 28.26 days. Patients receiving parenteral nutrition have a mean length of stay of 23.5 days. This contrasts with an overall average length of hospitalization for all patients of 14 days. Thus nutritional deprivation increases costs of hospitalization and the need for nutritional support.

Indications for Use

The most common conditions for enteral support include cerebral vascular accident, head injuries, accident/trauma, and protein calorie malnutrition. Additional indications for enteral nutrition are listed in Table 5. Indications for the use of parenteral nutrition support include accident/ trauma, intractable vomiting, protein-calorie malnutrition, gastrointestinal fistulas, pancreatitis, inflammatory bowel disease, short bowel syndrome, malabsorption and gastrointestinal surgery. Additional indications for parenteral nutrition are included in Table 6. The patency of the gastrointestinal tract is a major factor in the choice of either enteral of parenteral feeding.

In making the decision on how to treat the patient, a team of individuals screen and evaluate each individual for potential nutrition support. In a great majority, physicians (84%), dietitians (80%) and nurses (53%) are the primary individuals involved in deciding who will receive nutrition support. Oral feeding is always the first consideration; gastrointestinal tract patency seems to be one of the major criteria used in choosing oral, tube or intravenous feeding.

Ordering and selecting products for enteral feeding seems also to be done primarily by the physician or the dietitian or the physician and dietitian as a team. Although 78% indicated the dietitian most frequently selects products for enteral feeding, physicians are usually also involved. Supplies are ordered by the dietitian (53%) and/or the physician (48%). The physician (75%) and the pharmacist (60%) tend to select products for parenteral feeding. The physician (55%) and the pharmacist (50%) order the supplies for parenteral feeding. To a lesser extent the nurse is involved in all of these decisions.

Based on the results of this survey, age is clearly not a consideration in choosing a nutritional therapy. However, 45% of the respondents felt that mental status is a consideration in choosing nutritional therapy because of the increased likelihood of removing or pulling out a feeding tube (Table 7).

The issue of terminal illness as a contraindication to nutritional therapy was addressed. Seventy-nine percent of the respondents feel that terminal illness is not a contraindication to nutritional therapy in patients under age 65 and 77% felt nutritional therapy is not contraindicated in terminally ill patients over age 65.

The results of this survey suggest that most health care professionals believe that nutritional support should not be considered exclusively on the basis of age, medical condition or terminal illness. The medical condition, wishes or requests of patient or family, quality of life and potential for regaining some degree of health are critical considerations in a decision to continue or institute nutritional therapy.

The fact that 95% of respondents disagreed with the statement that "there is no point in using nutritional support in patients over 75 since they will die soon anyway," supports these conclusions.

On the statement "nutritional support is a life-prolonging technology and should be terminated when other life-support methods, such as respirators, are removed," there was a less clear feeling indicated by the respondents. Thirty-one percent disagreed, 44% agreed and 24% were unsure of their feelings on this item.

Respondents seemed to feel more strongly about the statement "starvation is an acceptable way of dying for the terminally ill patient." Sixty-two percent disagreed (38% strongly disagreed, 24% disagreed) and 17% agreed with this statement. Twenty-two percent were unsure of their feelings. However, 75% of the respondents believed that "nutritional support contributes to quality of life in terminally ill patients". Only 8% of the respondents disagreed with this statement.

It is clear that opinions vary on the statement "terminally ill patients should not have their lives prolonged by nutritional support." Seventeen percent strongly disagreed, 39% disagreed, 22% were unsure of how they felt, 18% agreed and 4% strongly agreed with this statement.

Side effects and unknown problems with nutritional support are not infrequent. Complications encountered frequently using enteral nutrition therapy are diarrhea, cramping, nausea and vomiting and pulmonary aspiration. Respondents reported the most frequently encountered complications of parenteral nutrition support are fluid/electrolyte disturbances, hyperglycemia, and catheter-related fever (Table 8). Fifty-three percent of the respondents indicated that they encountered complications more frequently in patients over age 65. Forty-four percent indicated that the complication range was the same in patients over and under age 65 and only 2% indicated that they encountered complications less frequently in their older patients. Ninety-three percent of the respondents indicated that patients who have multiple medical problems have more complications than those who do not. However, 96% of the respondents reported that multiple medical problems is not a contraindication to nutritional support. Generally there are no pre-established selection criteria for patients on enteral feeding (64%) and 57% of the respondents indicated that they do not have pre-established selection criteria for patients on enteral feeding. The health care practitioners who completed the attitude items support these conclusions.

Ninety-one percent of the respondents disagreed with the statement "nutritional support is dangerous to use in frail, elderly patients," (43% strongly disagreed, 48% disagreed). Ninety-five percent of the respondents disagreed with the statement "enteral feeding should not be used in elderly patients due to risk of aspiration pneumonia," (42% strongly disagreed, 53% disagreed).

When presented with the statement "elderly patients are too fragile to maintain on nutritional support," 90% of the respondents disagreed (54% strongly disagreed, 44% disagreed).

It is clear that management of patients requiring nutritional support is increasing in prevalence. Even in the over aged 65 many subjects requiring either parenteral or enteral feedings are sent home with nutritional support. Of particular interest is that a small group of health care professionals do not believe that older patients can be maintained at home with a nutritional intervention program. Even if this number is small (15-20%), the impact on hospitalization costs are enormous. For patients who are sent home, 48% reported that their solution was prepared by the patient and 54% indicated that the solution was prepared by a family member. For patients sent home on parenteral nutrition support, 61% reported that home nutrition support companies prepared the formula and 26% indicated that the hospital pharmacy prepared the formula for the patient (Table 9).

Age does not appear to be a factor in the decision to discharge patients from the hospital with either enteral or parenteral nutrition therapy.

An issue has been raised on the mechanism of storage for enteral and parenteral products. Most frequently enteral products are kept in the dietary department or on occasion, are kept in a general store room. Parenteral nutrition supplies and products are usually kept and stored in the pharmacy (89%) but on occasion they are kept and stored in the general store room.

The last item on the survey questionnaire was an open ended question inviting comments on nutritional support of the elderly.. The overwhelming majority of individuals who chose to comment indicated that they did not believe that age should be a factor in the access to or appropriateness of nutritional support therapy. Most felt that clinical conditions and the desire of the patient and family were the most critical factors in the decision making process. Other specific comments include:

(1) "All parenteral nutrition therapies undertaken in elderly and terminally ill patient coincide with some other form of medical intervention. Patients who are receiving comfort measures for the final terminal phase of an illness must be distinguished from the patient with terminal cancer who is obstructed in the GI tract but will receive palliative bypass surgery that will enable them to return home. The patient still

has terminal cancer but is not in the final phase and would possibly receive parenteral nutrition to shorten length of stay and facilitate wound healing."

(2) "Geropsychiatric patient profile: greater than 65 years old, underweight, multiple pressure decubiti, decreased muscle mass, decreased mobility, multiple joint contractures, unable to orally meet nutritional needs - most frequently exhibits decreased appetite and anorexia, decreased ability to tolerate even modified diet consistencies. Comments on nutrition: when I first came to this facility, I was amazed at the physical appearance of the geropsychiatric patients. Visible signs of long term protein-calorie malnutrition were evident. After much persistence and determination (i.e. educating physicians and overcoming resistance from other direct care staff) patients with aggressive nutritional support were showing improved wound healing, increased resistance to infection and increases in visceral protein status. Nutritional support in the elderly is most frequently overlooked in many instances due to: (1) ignorance of special nutrient needs of elderly patients; (2) lack of knowledgable personnel to consult, evaluate, monitor, and operate necessary equipment; (3) cost of products/equipment; (4) low priority of nutritional problems as compared to physical disabilities, failure to recognize potential relationships".

(3) "We have had several nursing home patients for whom hyperalimentation was necessary to correct nutritional deficiencies and gross malnutrition. The transition in the patient was extraordinary! - and well worth the cost."

(4) "Dehydration/starvation is a terrible way to die! Many times enteral tubes enable medications to be given which contribute to less painful deaths; also other medications which reverse illness."

(5) "Many elderly people are strong enough to overcome the crisis of illness and go on to resume their lives. It seems discriminatory to withhold nutritional support only because of age."

(6) "At our hospital the nephrologists and oncologists believe in providing nutritional support as needed regardless of age. Most of our patient population is elderly. Age is just not a consideration."

(7) "Enteral nutrition support is becoming more common place among our elderly patients, however, our major concern is initiating the appropriate nutritional support soon enough to improve the patient's prognosis."

(8) "I feel the elderly are discriminated against. DRGs limit patient stay and elderly frequently have chronic illnesses requiring longer stays and increased nutrition support needs. These needs are not being met because the patients are being sent home before illnesses have stabilized."

(9) "Many elderly patients thrive on nutrition support if only to let them die at home which is often their wish. I have seen patients that want to die but after nutritional intervention are glad to be alive."

(10) "Too often they are left without nutrition support of any kind while being bombarded with other forms of treatment."

(11) "It seems the outlook for the elderly involves discrimination against them through misguided transfer of questionable social policy and through medical decision making on the part of clinicians - unless we guard ourselves carefully."

(12) "I feel it would be a mistake to allow a patient to starve to death simply because they have reached the magic age of 65. Many factors must be taken into consideration, and policy makers must realize that patients cannot be placed in well-defined categories as easily as tax deductions can."

(13) "If patients are appropriately supported nutritionally, there will be less complications attendant to disease process and/or health crisis management."

(14) "This is a vital area and should be reimbursed by medicare-especially oncology patients with tube feeding."

(15) "Money spent on nutritional support in these patients is negligible compared to other medications and treatments performed in the last months or weeks of life."

(16) "Depends entirely on prognosis and present quality of life. I care for some young patients (less than 65) and reluctantly support them (because they are in a vegatative state). Yet I have treated elderly patients (greater than 75) who are alert, ambulatory and enjoy life even in the face of terminal illness. The process of dying is a phase of life, a time in life, when the dying person has a "job" to do. In the "job of dying" the person can get personal affairs in order, resolve conflicts with and between friends and relatives, and provide an example to survivors of the best way, the most productive way, to face death."

(17) "The increasing frequency (commensurate with increased government regulations) of admissions from extended care facilities of patients in irreversible starvation states and resultant complications due to malnutrition (i.e. decubitus ulcers). If support (i.e. enteral) is initiated then placement (extended care facility) is a serious problem. The questions are stated in black and white. There is no allowance for the "gray" area encountered in each individual case. There are a number of variables not addressed in this questionnaire concerning nutritional support of the elderly. One area omitted is the important issue of the impact of government regulations. We hope these issues are also addressed, as this information or input from practitioners is vital in the government process concerning nutritional support of the elderly."

(18) "We live in a rural area with a high population of elderly. I feel that appropriate nutritional support can decrease recovery time from illness and

improve their quality of life. Patients are easier to wean from ventilators if they have been nutritionally supported."

(19) "As with dialysis - I do not feel it should be administered just because it is available and someone will pay for it until death."

(20) "Very important; need research to determine nutritional needs of populations 60 to 74, 74 to 85, 85 + and functional methods to assess nutritional status."

(21) "I feel the elderly have the right to benefit from nutritional support just as the young person does. Unfortunately, the elderly suffer some form of discrimination due to the fact that they are probably on medicare and medicaid and reimbursement for all nutritional therapies is low."

(22) "There are ethical issues which must be resolved especially with respect to the use of parenteral nutrition in the aged person who has no supportive family."

(23) "Need certification/training for nursing homes to handle and State review boards to approve tube feedings."

(24) "Under DRGs scheme I see elderly patients decline in health or actually stay in hospital with more complications and therefore high cost secondary to hesitance to use early nutrition support because of concern of costs."

"Just because someone is old and unable to eat, I don't believe we can allow them to starve to death. That is low, miserable death to someone who is frightened and doesn't understand. If the government doesn't want to support this fast growing group, then they should develop a quick, painless death!"

From the above comments it is clear that educated health care professionals involved in nutrition management feel strongly that there is a definite place for nutritional support of the elderly, irrespective of their age, medical status or closeness to death. The data, however, is both anecdotal and emotional. There clearly are multiple unresolved questions both from a management, efficacy and ethical standpoint which need to be addressed. These will be expanded upon later under a section on research needs.

Utilization in Nursing Homes

The use of enteral and parenteral nutrition in nursing homes for critically and terminally ill patients is a more difficult area to document accurately. The American Health Care Association, with support and guidance from the American Society for Parenteral and Enteral Nutrition surveyed 8500 nursing homes and other long term care facilties to gather information on the utilization of enteral and parenteral nutrition. Data presented will be a compilation of the results of that survey (the AHCA survey collected data from 316 respondents) with two respondents in the survey conducted by us who are employed by long term care facility chains.

According to a market research survey conducted by CH Kline and Company, 533,400 patients in nursing homes received some type of enteral nutrition therapy during 1984. This same data indicated that 15,600 patients in nursing homes received parenteral nutrition support during the same period of time. The actual incidence remains difficult to determine. The 316 facilities who responded to the AHCA survey indicated that they currently had 1,159 patients receiving enteral nutrition while the respondents to our survey indicated a total of 2200 patients in their nursing home facilities. One of our respondents directs care in 110 long term care facilities. They average 1,000 patients receiving enteral products per month (9 patients per facility per month). This same respondent indicated that 10% of all patients over the age of 65 receive enteral nutrition support. They indicate that in 110 facilities they have 10,000 beds. Of those, patients receiving enteral nutrition, 100% were over age 65. A very high proportion of patients receive oral supplementation.

The AHCA survey respondents indicated a total of 57 patients presently receiving parenteral nutrition support. The two respondents to our survey indicated that parenteral feeding was relatively rare with 2-8 patients receiving parenteral nutrition per month. One hundred percent of patients receiving parenteral feeding were over age 65.

The professional costs are of course much less. Physician involvement is very limited and even contact with other nutrition experts is quite rare.

Seventy-five percent of the respondents to the AHCA survey indicated that they had access to consultation regarding enteral and parenteral nutrition. Consultation is usually provided by nutrition support teams in local hospitals or by manufacturers' representatives. Large nursing home chains usually have regional office staff who serve as resources for individual facilities.

It seems fairly certain from these data that the use of enteral nutrition support in nursing homes is much more common than the use of parenteral nutrition support. Use of intravenous hydration therapy and intravenous medication therapy does seem to be fairly common. The skilled nursing care required for starting an i.v. is usually accessible in nursing home facilities.

The guidelines for enteral support used in the institution setting are similar to that of acute hospitals for the more common indications. It is clear that an inability to feed onself is the major indication of enteral hyperalimentation. In this regard cerebral vascular accident constitutes the most prevalent indication. Other neurologic disorders, particularly end stage dementia caused by Alzheimer's disease or other disorders, may necessitate nutrition intervention. Frequently protein calorie malnutrition may be present at the time of admission or may develop during institutionalization, and this may necessitate nutritional support. Secondary protein calorie malutrition due to a primary, incurable disease may be present and require nutritional intervention.

It is noteworthy that one of the respondents indicated no conditions for which parenteral nutrition is used. This reflects the limited use of this technique in the nursing home setting.

Mental status is an important variable in choosing the type of therapy to be provided. In the nursing home setting these patients run the risk of pulling out feeding tubes. In this regard guardians are frequently needed to obtain consent. Patient or family consent is usually one of the deciding factors in the institution or continuation of nutritional support therapy. Written consent from a responsible family member or the patient himself is usually required prior to the institution of therapy or a decision regarding cessation of nutritional support therapy. Willingness to use aggressive nutrition support in these patients may be limited by a consideration of the quality of life provided. In many of the responses to both the AHCA survey and the survey conducted by us, quality of life is a major consideration.

Complications encountered with enteral nutrition include aspiration pneumonia, diarrhea, tube insertion site inflammations, skin excoriation, dehydration, fluid/electrolyte disturbances, nausea and vomiting. The complications associated with total parenteral nutrition in the nursing home seem to be limited to inflammation around the catheter insertion site (a sign of infection), and problems with restraining the patient to avoid removal of the catheter. Adequate staff time needed for dressing changes is frequently a concern.

Major problems in relation to nutrition in nursing homes are firstly re-imbursement and secondly staffing patterns. Payment for total parenteral nutrition services are frequently delayed until annual cost reports are filed, causing cash flow problems and frequent inability to purchase expensive fluids and equipment.

Alternative methods of feeding in nursing homes often require additional staff time. Patients who require hand feeding may wait for extended periods of time for someone to have the time required to feed them their meals. Sometimes this results in cold, unappetizing food which is then refused by the patient. A frequently used alternative to regular meals in nursing homes is oral enteral supplements. It is assumed that taking nutrition in liquid form is more easibly managed by patients who may have difficulty in managing knives and forks. Problems do arise with patients who do not have the strength or manual dexterity to open cans or pour formula into a glass or cup. Consumption of oral enteral feedings is often assumed and not monitored carefully. Providing cans of oral supplements with meals does not necessarily indicate consumption. In addition, even if consumed, many oral enteral supplements are low in residue and may contribute to a generally recognized problem of constipation. Adequate fluid intake is a serious problem in nursing home patients. Providing fluids that are nutrient dense, although they contribute greatly to overall nutritional intake if consumed, does not solve the problem of inadequate fluid intake. Difficulties in keeping staff knowledgeable about procedures when nutrition therapy is used infrequently and sporadically is a concern. Problems also arise in convincing social workers and physicians that skilled nursing facilities can provide adequate care for nutritionally supported patients. This is concomitant with a problem frequently encountered in nursing home facilities regarding 24 hour registered nurse coverage. Often there is only one registered nurse covering per shift, usually during the night, which is inadequate to properly monitor and maintain enteral or parenteral lines.

It is possible to extrapolate from the data on hospitalized patients that nutrition support contributes greatly to the quality of life of most patients. It has been specifically stated on multiple occasions that nutritional support contributes to the prevention of decubitus ulcers by providing adequate nutrients and protein to maintain tissue and skin integrity. For patients who have developed decubiti related to long term malnutrition and improper or inadequate nursing care, nutritional support often provides enough substrate to aid in the healing of wounds by providing protein and energy to make new tissue.

It is really quite clear that staffing patterns even in skilled nursing facilities are often inadequate to provide sophisticated parenteral nutrition support, although the use of enteral tube feeding and i.v. hydration is more common. Additional staff training and possible certification should be required to insure that both enteral and parenteral therapies are delivered safely and appropriately to extended care facility patients.

Although not specifically stated, many skilled and extended care nursing facilities do not institute therapy but accept patients discharged from hospitals who are being supported with one of these techniques. Often patients who are malnourished and dehydrated will be transferred to acute care hospitals for resolution of the problem and the nutritional support modality is begun in the hospital. Patients are generally not transferred out of acute care hospitals until their condition has stabilized.

There has been no discernible research conducted to answer the questions of nutritional support in nursing home facilities. Most research in this area has been performed in acute care settings. When presented directly with the problem of allowing patients to die of starvation or dehydration, the response is overwhelmingly against allowing this to happen. However, death by starvation and/or dehydration may occur due to simple neglect, oversight, or lack of understanding of the process as it is occurring.

RESEARCH NEEDS

It is clear that little attention has focused on the nutritional needs of the older individual in general or specifically on the nutritional needs of the terminally or critically ill older individual. Many unanswered questions remain with regard to developing a rational approach to an appropriate and effective management of these individuals. In this regard the following research areas require critical attention:

1. Standards for the Elderly. It is clear that the lack of appropriate standards for anthropometric, biochemical, hematologic and vitamin nutrient status measurement make interpretation and diagnosis of malnutrition in the elderly particularly difficult. It is very important that normal values are needed that are adjusted for age and the physiologic decline in function that occur with age. Although some data is available at the current time these are derived from extremely small population groups that do not reflect the broad ethnic range of individuals likely to be seen in hospital settings in the United States.

Appropriate standards of normality for hospitalized individuals are also important. It is clear that the presence of disease can alter parameters usually employed to assess nutritional status. For example, both serum albumin and transferrin (frequently employed markers of visceral protein nutritional status) act as acute phase reactants and drop significantly in the presence of acute disease. The modulating effect of disease on nutritional parameters must be studied so that one can dissect out an abnormality that is disease or nutrition related.

2. Nutritional Requirements for the Elderly. Although receiving some recent attention there still is a great deal of controversy in regard to the energy, protein and single nutrient requirements of older people. While this is currently being addressed by various groups, additional

efforts in this regard are essential. Most critical is an accurate documentation of the protein needs of older people. A clear-cut recommendation of the protein/calorie ratio in healthy older subjects is still a matter for debate. There is good evidence in the literature that the presence of disease markedly increases catabolism and causes substantial increases in protein requirements. There is anecdotal evidence that when ill individuals of any age are supplemented they should receive the greatest fraction of calories as possible as protein. Exactly what protein intake should be in older terminally or critically ill indviduals requiring nutrition support remains to be determined. Evidence of clear documentation of appropriate nutritional support needed to maintain adequate nutrient levels and to prevent catabolism and other sequelae of nutritional deprivation is still controversial and requires more attention. The exact formulation of enteral and parenteral feeding solutions in older individuals who require either short or long term nutritional maintenance is still unknown. Furthermore, the degree to which older people should be supplemented with vitamins, trace minerals, calcium and other key nutrients remains to be determined.

3. Diagnosis of Malnutrition. Although anecdotal evidence is usually presented for the criteria of the diagnosis and detection of malnutrition in older individuals this area requires additional investigations. The reliability of serum albumin or other hematological markers as screening tools for the detection of protein energy malnutrition remains controversial. The close similarity between structural and functional changes that occur with normal aging and those which occur because of the presence of nutritional deficiencies make the interpretation of individual parameters difficult. Further studies on the accurate detection of malnutrition in the elderly are critical.

4. Management. The indications for enteral and parenteral feedings, although on the surface relatively clearcut, are still open to debate. There is recent evidence that enteral hyperalimentation is more risky than previously reported. In the elderly, the potential risk of aspiration pneumonia cannot be underemphasized. An additional concern relates to the fact that the trend towards nasogastric feeding, and its ease of performance in the sedated individual, gives risk to the potential of abuse. Further studies accurately documenting clearcut indications for enteral and parenteral hyperalimentation are essential.

5. Efficacy of Interventions. Even if nutritional therapies are commenced in the critically or terminally ill older individual, their efficacy remains to be documented. The impact of nutritional support on parameters of nutritional status, such as visceral protein stores, and host defense are still not clear. The ability of ill older individuals to increase muscle mass as a result of the correction of nutritional intervention remains to be determined. Furthermore careful studies documenting the impact of nutritional status on quality of life will greatly assist in documenting the need for this form of medical intervention.

6. The Role of a Comprehensive Health Care Program in Optimizing Health. It is clear that nutritional intervention constitutes a small part of the total management of the older patient. Studies need to address the interrelationship between nutritional support and active rehabilitation programs, including attention to physical activity and psychosocial well- being are critically important. The potential role of improving social circumstances in delineating risks of malnutrition should also be considered.

7. Cost/Benefits Ratio Studies. There are critical research needs in determining the cost/benefit of nutritional intervention of older individuals.

It is a reasonable hypothesis that the prevention or correction of nutritional deficiencies will improve health and well being, decrease the risk of institutionalization, diminish the need for acute hospital admissions, and improve either the quality or quantity of life. In this regard the potential role of community based nutrition survey and intervention programs are areas for study. This is a particularly important consideration for "at risk" populations. In this regard, home bound older individuals who have multiple medical problems, poor social circumstances, or who require assistance with their meals should be considered for monitoring. In addition, it is generally accepted that older institutionalized individuals are at risk of developing nutritional deficiencies. The potential role of screening for nutritional deficiencies, monitoring nutrient intake and the prevention of nutritional abnormalities can be studied.

8. Staffing Needs for Nutritional Therapies. In the acute care hospital setting it is apparent that staff patient ratios allow the easy administration of nutritional intervention. In contrast, it is clear that the staffing patterns of long term and chronic care facilities are not ideal for nutritional support. As nutritional intervention requires additional hospital stays it is likely that more and more of these patients will be referred to chronic care facilities for further management. In order to document the impact of this referral pattern, studies examining the potential staffing needs of institutionalized older individuals requiring nutritional support should be considered.

TABLE 1 YEARS IN PRACTICE OF RESPONDENTS

YEARS	# RESPONDENTS
0-4	81
5-9	180
10-14	100
15-19	53
20-24	25
25+	22

TABLE 2 SIZE OF INSTITUTIONS

SIZE	# RESPONDENTS
Under 100	21
100-249	85
250-499	146
500-1000	152
1000+	35

TABLE 3 TYPE OF INSTITUTION*

TYPE	# RESPONDENTS
Critical Care	183
Private	169
University	108
Federal	53
Chronic Care	45
Community	188
State Government	21
Other**	

* Respondents were instructed to check as many as apply.

** Others include county, home health, research, health maintenance organization.

TABLE 4

COSTS OF PARENTERAL AND ENTERAL NUTRITION SUPPORT

PRODUCT/SERVICE	X COST	RANGE	N
Liter Enteral Solution	$9.70	$1.10 - $42.00	307
Enteral Support*	$42.88	$4.00 - $132.00	219
Liter Parenteral Solution	$71.00	$10.00 - $250.00	313
Parenteral Support*	$196.00	$25.00 - $500.00	254

* Includes solution, equipment, supplies, personnel

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TABLE 5 MOST COMMON INDICATIONS FOR ENTERAL NUTRITION SUPPORT

CONDITIONS	# RESPONDENTS INDICATING USE (N = 469)	
	#	%
Protein Calorie Malnutrition	373	81
CVA	362	79
Head Injuries	320	70
Accident/Trauma	312	68
Cancer Chemotherapy	299	64
Cancer Radiotherapy	291	62
Sepsis	289	62
Renal Failure	280	60
Head/Neck Obstructions	278	59
COPD	276	59
Hepatic Failure	271	58
Esophageal Obstructions	248	53
Wired Jaw	225	48
Long Bone Fractures	217	46
Thermal Injury	207	44
GI Surgery	203	43

TABLE 6 MOST COMMON INDICATIONS FOR PARENTERAL NUTRITION SUPPORT

CONDITION	# RESPONDENTS INDICATING USE	
	#	%
Inflammatory Bowel Disease	393	86
GI Fistulas	377	82
Short Bowel Syndrome	360	79
Pancreatitis	349	76
Malabsorption	336	73
Intractable Vomiting	329	72
Accident/Trauma	327	71
Protein-Calorie Malnutrition	323	71
GI Surgery	323	71
Sepsis	307	65
Renal Failure	299	64
Esophageal Obstructions	298	64
Cancer Chemotherapy	292	62
Hepatic Failure	284	61
Maldigestion	271	58
Cancer Radiotherapy	248	53
Head/Neck Obstructions	228	49
Head Injuries	207	44
Fluid/Electrolyte Disturbances	204	43

TABLE 7

Mental Status as a Factor in Selection of Nutritional Therapy.

n = 438

	Yes	No
#	196	242
%	45%	55%

Reasons cited by "Yes" respondents (N-111)*	N
Patient liable to pull out tube/catheter	52
Safety/need help with care	25
Lack of cooperation	23
Prognosis poor	18
Disoriented/confused	17
Mentally/incompetent not eligible for payment	8
Need special nutritional products (ie. for hepatic encephalopathy)	6
Unable to feed themselves	12

*Respondents who indicated that mental status is a factor in choosing therapy were asked to explain why.

TABLE 8 MOST COMMONLY REPORTED COMPLICATIONS ENCOUNTERED WITH ENTERAL AND PARENTERAL NUTRITION

Enteral Nutrition	# Reporting Problem
	n = 458	

	#	%
Diarrhea	424	93
Nausea/Vomiting	354	78
Cramping	341	74
Pulmonary Aspiration	341	74
Fluid/Electrolyte Disturbances	284	62
Hyperglycemia	265	58
Hyponatremia	216	47
Parenteral Nutrition		
Hyperglycemia	399	87
Fluid/Electrolyte Disturbances	375	82
Catheter-Related Sepsis	371	81
Fever	348	76
Hypophosphatemia	337	74
Hypokalemia	322	70
Hyponatremia	310	68
Hyperkalemia	299	65
Pneumothorax	298	65
Hypomagnesemia	253	55
Subclavian Vein Thrombosis	253	55
Hypernatremia	239	52
Hypoglycemia	234	51

TABLE 9 PREPARATION OF HOME FORMULAS

n = 458

	#	%
Enteral		
Prepared by Patient	221*	48
Hospital Pharmacy	18	4
Family Member	247	54
Home Nutrion Support Company	181	40
Other	15	4

n = 458

	#	%
Parenteral		
Prepared by Patient	39*	2
Hospital Pharmacy	119	26
Family Member	57	12
Home Nutrition Support Company	279	61
Other	9	-

* More than one answer was given by respondents.

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NUTRITIONAL SUPPORT AND HYDRATION
FOR
CRITICALLY AND TERMINALLY ILL ELDERLY

The Oley Foundation, Inc.
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Albany Medical Center
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TASK 1.

TECHNIQUES FOR NUTRITIONAL SUPPORT AND HYDRATION

Introduction

Enteral or parenteral nutritional support is an important therapy for anyone, including someone 65 or older, who is unable to meet his nutrient needs with meals and snacks due to inadequate ingestion or impaired digestion or absorption. Although "enteral," which theoretically means feeding via the gut, includes normal eating, in the current context of very technical nutrition therapy, enteral feeding refers to the infusion of a liquid nutrient formula by tube into the upper gastrointestinal tract. "Parenteral," which means outside the gut, in this context refers to the infusion of nutrient solutions via a catheter into the bloodstream. Figures 1 and 2 show several patients receiving enteral or parenteral infusions and give a general picture of the technology. The following sections discuss these two nutritional techniques in more detail, outline some aspects of the technology from the patient perspective, and explore some issues for the future.

Enteral Techniques

The first record of tube feedings is reported to be in the 16th century when Capivacceus introduced nutrients into the esophagus by tube.[1] Today enteral feeding tubes are placed either through the nose or through an ostomy, a medically created tract, into the gut. The development of small bore, pliable feeding tubes that remain soft with continued exposure to digestive juices has made long-term tube feeding possible. Figure 3 shows the most common placement sites and Figure 4 shows how a nasoenteric tube may be secured in an uncooperative patient. In Table I the placement techniques of the different tubes, their clinical uses, and their advantages and possible drawbacks are summarized. (Also see Appendix A(1) for a listing of some brands of tubes currently on the market with their manufacturers, characteristics, and list price.)

In addition to the feeding tube, enteral nutrition requires careful regulation of the nutrient infusion rate. Rapid infusion may provoke gastric regurgitation with aspiration into the lungs, vomiting, or diarrhea. Too slow an infusion may result in inadequate hydration and nutrient deficits. Enteral feeding pumps assure the most uniform delivery of the formulas and Appendix A(2) lists some of the available models with their features.

Pumps are not always used for patients receiving tube feedings. If the distal end of the feeding tube (nasogastric or gastrostomy) is in the stomach and the gut is functioning normally, bolus feeding (i.e., quantities of 300-400 cc. administered in a single dose with a large syringe) may be used. In this case the stomach serves as a "reservoir" for the food which slowly passes into the intestine to be digested and absorbed.

"Gravity drip" is another method of administering tube feedings. In this method, the height the formula container is hung provides the force and a regulator clamp calibrated by counting the drips controls the flow rate. However with gravity drip, accurate regulation depends on hourly monitoring of the flow rate by a nursing attendant or, depending upon the setting, a family member or the patient himself.

The duration of enteral infusion can range from one to 24 hours per day and the formulas are an excellent media for proliferation of bacteria from both internal and external sources. If a formula is to be infused over many hours without constantly refilling the container, it is important that the nutrient mixture be kept cool and protected from contamination. Complications arising from contamination of enteral formulas are diarrhea, enteritis, and bacteremia.[2-6] Preventing these problems requires an infusion container that can hold a large volume of formula (1-3 liters), that is closed, to protect the solution from airborne contaminants, and is kept cool to limit the growth of any organisms. In the past, such containers used to be large glass burettes or metal chambers with a cooled stirring device. Recently such containers have been replaced by disposable plastic bags that are closed to the atmosphere and some have built-in ice packs to keep the nutrient solution well below room temperature. (Appendix A(2) includes brands of enteral formula containers.)

Another potential complication from tube feedings is aspiration pneumonia. Aspirating stomach contents that have been regurgitated or vomited can bring on acute respiratory distress. Regurgitation can occur quite subtly, particularly in those with impaired mental status or with decreased ability to close their glottis (as in someone with a tracheostomy). One measure that can be taken to decrease potential aspiration is to make sure the patient's head is elevated to 30 degrees at all times. Other measures include checking the tube's placement, checking gastric residuals, and initially diluting formulas to encourage gastric emptying.[7]

Enteral formulas cover a wide spectrum. They range from those that are produced at home by blenderizing normal table food to formulas that have a defined chemical composition tailored for a specific metabolic disorder, such as those enriched with branched chain amino acids and reduced in aromatic amino acids for patients with hepatic failure. Table II summarizes the various enteral formula categories, their clinical indications, and methods of administration. (See Appendix A(3) for some of the commercially available enteral products with their manufacturers and price per liter.)

Parental Techniques

The development of an "artificial gut" or total parenteral nutrition (TPN) began in the 1960's when Dudrick and his colleagues conducted the first experiments to show that growth, development and positive nitrogen balance can be achieved in humans through parenteral feedings.[8] Because of its complexity and potential risks, TPN was initially undertaken only in the hospital setting. In 1969 Shils and associates[9] sent the first patient home and in the past 10-15 years the experience of managing patients at home on parenteral nutrition has grown rapidly.[10-13]

As defined earlier, parenteral nutrition* is the technology of infusing nutrients via a catheter direclty into a vein. Figure 5 shows examples of parenteral feeding catheters (also called "lines") and Appendix B(1) gives a more complete list of some brands that are currently on the market.

Because parenteral nutrient solutions are highly concentrated solutions, they are not readily tolerated by small veins with low blood flow, hence the catheters must be threaded into large, high flow, central veins where the infused solution can be rapidly diluted. Figure 6 shows the veins that can be used for accessing the central venous system and Table III summarizes the various characteristics of the catheters, both the externalized lines and those with subcutaneous portals, and the technique of insertion. Figure 7 depicts a typical venous catheter placement.

---

*Occasionally TPN is referred to as hyperalimentation, a former term for the technique.

With parenteral feeding, a constant and accurate infusion rate is even more critical than with enteral feeding and pumps have been developed to perform this task. Appendix B(2) lists some of the models currently available for parenteral feedings. Among their special features are a battery to insure that power failure does not interrupt infusion and alarm devices to warn nursing attendants or patients about air bubbles or occlusions (i.e., resistance to flow that could mean a kink in tubing or a clot).

Each infusion formula provides several standard components: protein (amino acids), dextrose, fatty acids or lipids, electrolytes, trace elements, and vitamins. However, the formula must be adjusted to the specific needs of each patient and laboratory tests are necessary to monitor the adequacy of the therapy. For example, in a patient with renal failure, the amino acid component may be modified to provide principally the essential amino acids (the ones the body cannot manufacture) and restrict the sodium, potassium, phosphorous, and minerals; whose excretion is defective in renal impairment.

Table IV presents a standard parenteral nutrition formula. This formula provides all the known nutrients except iron. Traditionally iron has not been included because of early reports of parenteral iron causing life-threatening anaphylaxis and because many hospitalized patients receive generous iron supplements from blood transfusions. In recent years there has been a growing experience with including small amounts of iron (1-3mg/day) in the daily solutions and this appears to be safe.[14,15] (See Appendix B(3) for a list of parenteral solutions, their manufacturers, and list prices.)

Because parenteral formulas usually provide the required calories primarily as dextrose, they are highly osmolar solutions. In the immediate vicinity of the catheter tip, these highly osmolar solutions impair action of the phagocytes, cells that attack foreign particles by surrounding and engulfing them. Parenteral formulas are also potential growth media for contaminating organisms, bacterial and fungal. Since they are infused close to the heart and since local defense mechanisms are impaired by virtue of the osmolarity, it is easy to understand that the central danger of parenteral feeding is blood borne infection or sepsis. For this reason aseptic technique in compounding the formula, setting up the infusion system, and handling the venous catheter is mandatory.

Table V summarizes the potential complications with parenteral nutrition, especially at the outset of instituting the therapy. For long-term patients at home on parenteral support, micronutrient deficiencies become a more significant issue and these complications will be discussed in the section on home utilization.

Patient Perspective

To accept and benefit from the techniques of enteral or parenteral nutritional support it is important that all aspects of the technology be discussed with the patient and the patient's family before therapy is instituted. The family discussion is particularly important if the patient is senile, comatose or if the patient must rely on family members to assist with the regimen. For both the long-term or short-term patient and their families, this discussion should encompass:

1. An explanation of why the specialized nutritional support is indicated, what benefits can be anticipated, and how long it may be necessary.
2. Information on catheter (line) or tube placement. This should include: a) the type of device to be used; b) site of entry and anatomical location inside the body; c) lubrication or type of anaesthetic used; d) position of patient during insertion and patient's role to ensure ease and safety of the procedure; e) potential discomfort and hazards associated with the line or tube; and f) how the line or tube is changed or removed.

Particularly relevant for the long-term patient, especially one discharged to the home is:

1. What and who will be involved in the daily care of the tube (clean technique) or catheter (aseptic technique) and dressing changes.
2. Use of the pump and taking advantage of its special features to aid in controlling the infusion process.
3. Preparation and storage of the nutrition formula.
4. Potential complications and how to manage them appropriately.
5. Inventory and reimbursement management, including supply ordering, cost and payment mechanisms.
6. Details of 24-hour emergency back up for medical complications or equipment breakdown.
7. Development of a plan for post-discharge medical follow up.

Future Developments

The Small Pump for Greater Mobility

Since nutritional rehabilitation is only totally successful if the patient is restored to the maximum level of activity that he or she may be capable of, it is usual for patients discharged from the hospital on long-term parenteral or enteral therapy to obtain the nutritional support overnight. This permits the patient to be free from pump, tubes, and solutions during the day. In many patients with bowel disorders requiring therapy, there is an abnormal loss of gastrointestinal secretions so that these patients are subject to severe dehydration. For this reason toward the end of their "off" period, they become very dry and uncomfortable. Conversely, when the infusion restarts and hydration is restored, they start to produce urine and must get up and go to the bathroom several times during the night. Obviously this presents a dilemma in the older patient who wants daytime mobility but may require close supervision for the infusion period and need help in going to the bathroom when infusing.

There is a "vest" with a small battery pump (see Appendix A(2)) that permits ambulatory parenteral infusion. So far this device has proven useful in extending the day for active adults, but has not been developed to the point where it is a true alternative to the large volume, nocturnal infusion. Clearly, however, it is a step in the right direction.

Simplification of the Parenteral Nutrient Solution

In the early years of developing intravenous fat solutions there was a major problem of stabilizing the fat particles and avoiding their coalescence into large particles that could induce a syndrome akin to fat embolism.[16] Recently a number of studies indicate that it it safe to premix the fat solution with the other parenteral compounds producing a "three-in-one" infusion (fat, dextrose, and amino acids in one mixture).[17,18] More studies are needed to evaluate how long such solutions are stable for certainly using a "three-in-one" solution simplifies delivery, which is especially valuable for the older, less dexterous individual.

Micronutrient Composition

While the adequacy of calories, protein and fluids is fairly easy to assess clinically, the requirement for micronutrients such as trace elements, vitamins and essential fatty acids are harder to establish and more studies are needed. Since nutritional therapy utilizes plastic bags, tubing and filters, adherance of nutrients to these materials has to be evaluated. In addition, as parenteral feeding is into the systemic rather than the more physiologic portal system, nutrients may be presented more rapidly to the kidney than to the liver, the organ commonly involved with storage and metabolic activation of nutrients. For this reason, parenteral requirements may be higher than the amounts established for oral feeding. Also, as stated earlier, many gut disorders are associated with the abnormal loss of enteral secretions that can result in the abnormal endogenous loss of many nutrients and interruption of normal enterohepatic cycles (e.g., cobalamin, folic acid, vitamin D, zinc, calcium, magnesium, copper, and perhaps other nutrient conservation is impaired).

One future approach to studies on trace element requirements may be autopsy analysis of the tissues of patients who have been on nutritional therapy for many years. Another approach to altered nutrient metabolism may be stable isotope tracer studies.

Enteral Therapy

Enteral therapy is clearly a less expensive form of nutritional support than parenteral therapy. With the advent of more comfortable feeding tubes and conviently packaged enteral formulas, there has been a greater use of enteral support in many gastrointestinal disorders. More information is required at both a basic and applied level about how to make enteral feeding truly successful. A key issue will be better reimbursement practice by third party payers. Currently the reimbursement for enteral therapy is so uncertain that it positively encourages the more expensive parenteral approach. From the patient and family perspective it is certain that no one would cooperate with either form of therapy if they did not experience substantial benefit. Both types of therapy are cumbersome and restricting so flagrant abuse of nutritional support is unlikely and a far cry from the era of "tonics." However, its widening application beyond the hospital setting requires that appropriate professional standards and quality of care be monitored.

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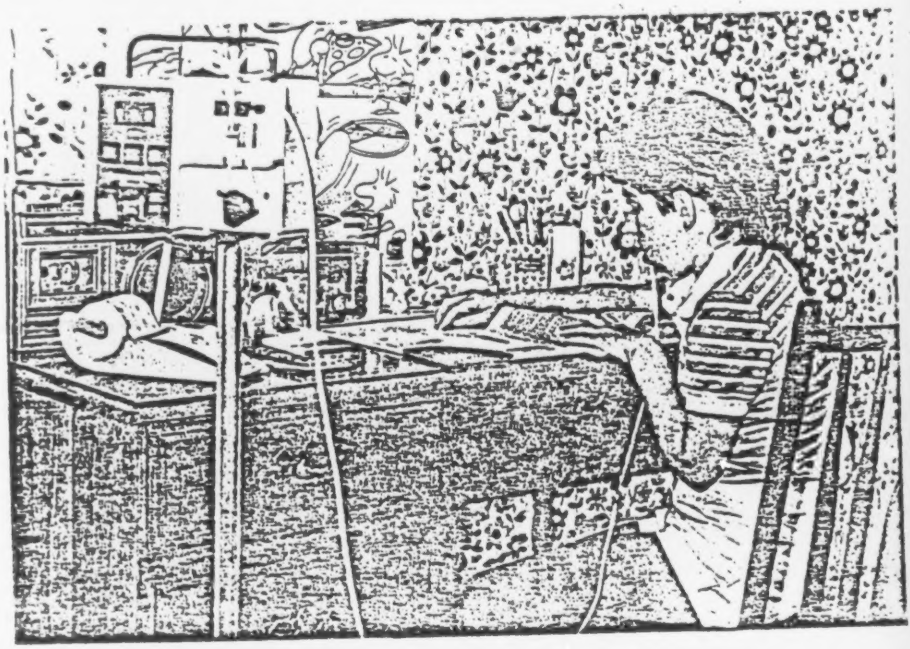
FIG. 1. THREE PATIENTS RECEIVING ENTERAL FEEDINGS IN THREE SETTINGS.

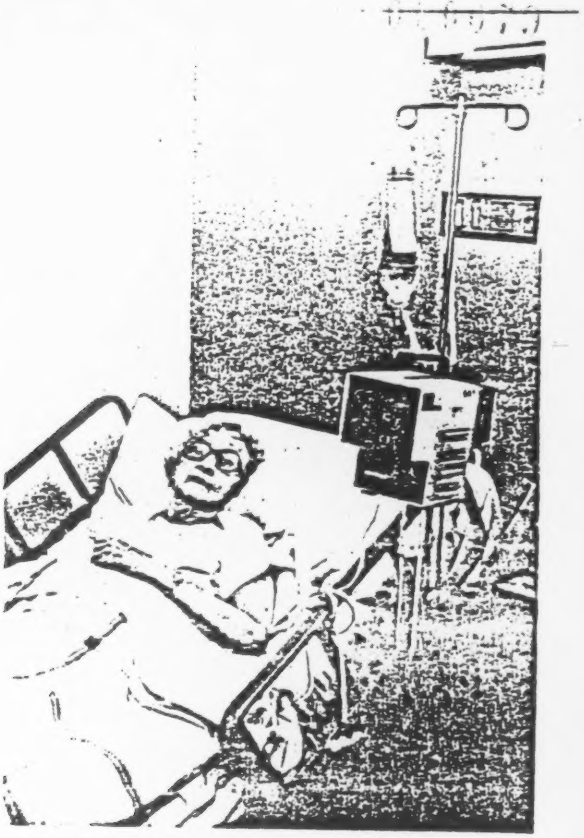


1a. Crohn's patient receiving feeding at home through nasogastric tube inserted daily by patient.

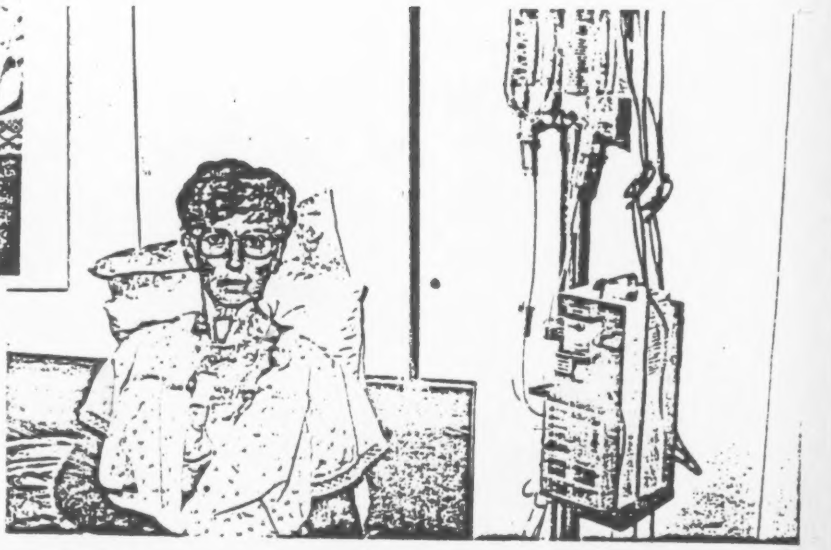
1b. Hospitalized patient receiving enteral feeding for anorexia nervosa.

1c. Stroke patient receiving feeding at nursing home through gastrostomy (tube into stomach). Tube in throat is tracheostomy to aid breathing.

Fig. 2 TWO PATIENTS RECEIVING PARENTERAL FEEDINGS IN TWO SETTINGS.



2a. Crohn's patient receiving parenteral nutrition via indwelling catheter (Hickman) in hospital



2b. Radiation enteritis patient receiving parenteral infusion at home via subcutaneous reservoir catheter. (Above: catheter site and tubing; right: pump and nutrients.)

80

FIG. 3. COMMON PLACEMENT SITES FOR ENTERAL FEEDING TUBES.

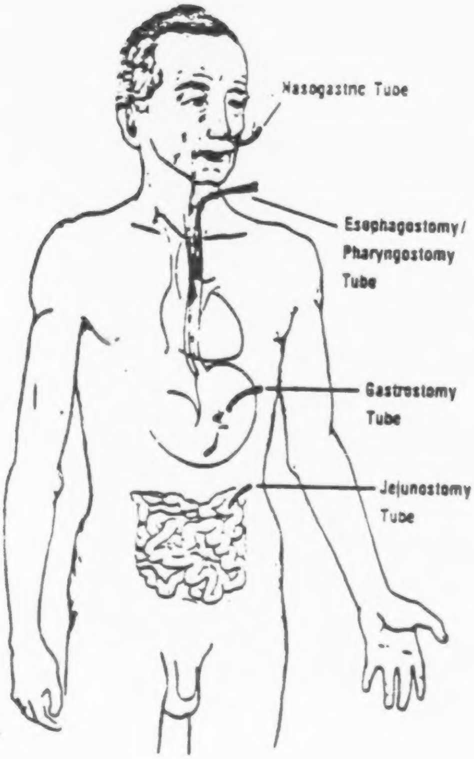


FIG. 4. TECHNIQUE FOR SECURING NASOENTERIC TUBE IN AN UNCOOPERATIVE PATIENT.

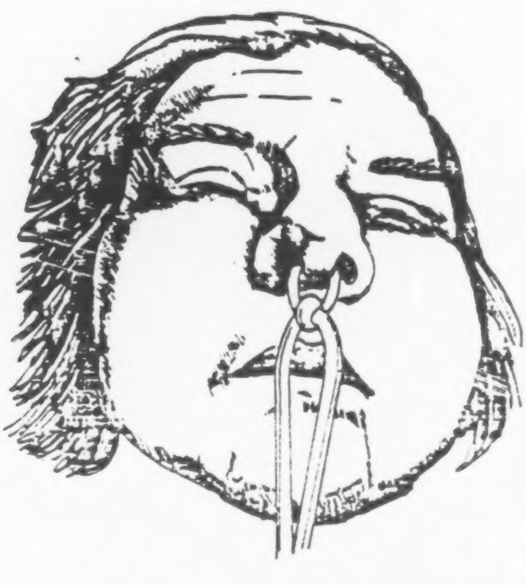
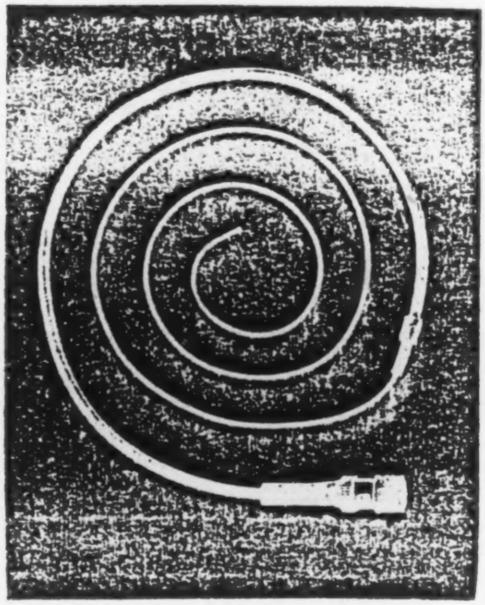
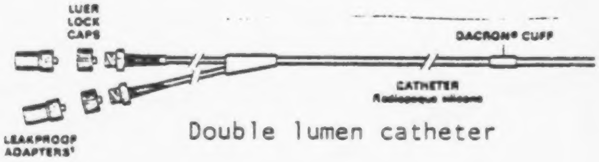


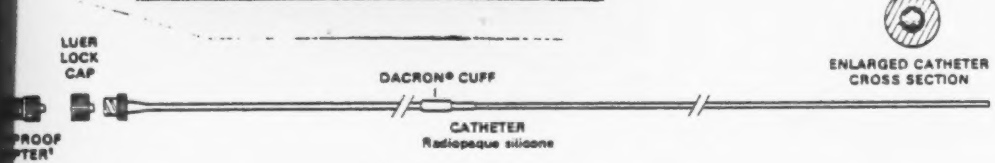
FIG. 5. PARENTERAL NUTRITION CATHETERS.



5a. Externalized catheters.

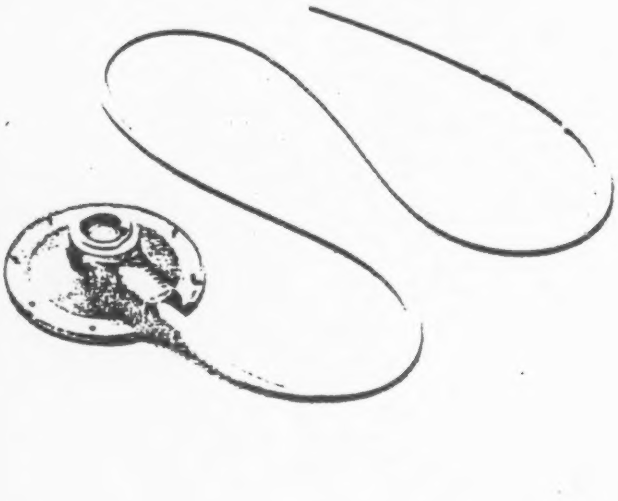


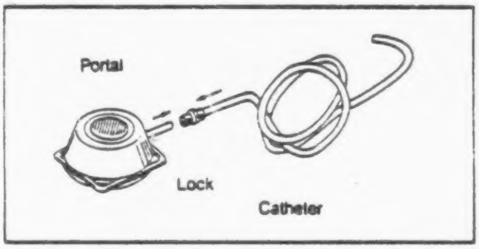
Double lumen catheter



, (showing the lumen)

5b. Catheters with subcutaneous portals.
Lower right is a cross section
of an implanted portal.





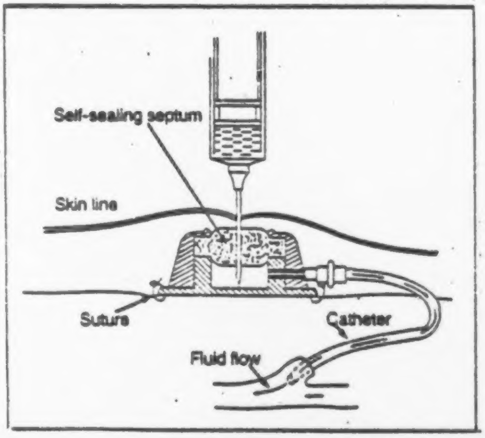


FIG. 6. ACCESS VEINS FOR PARENTERAL FEEDING.

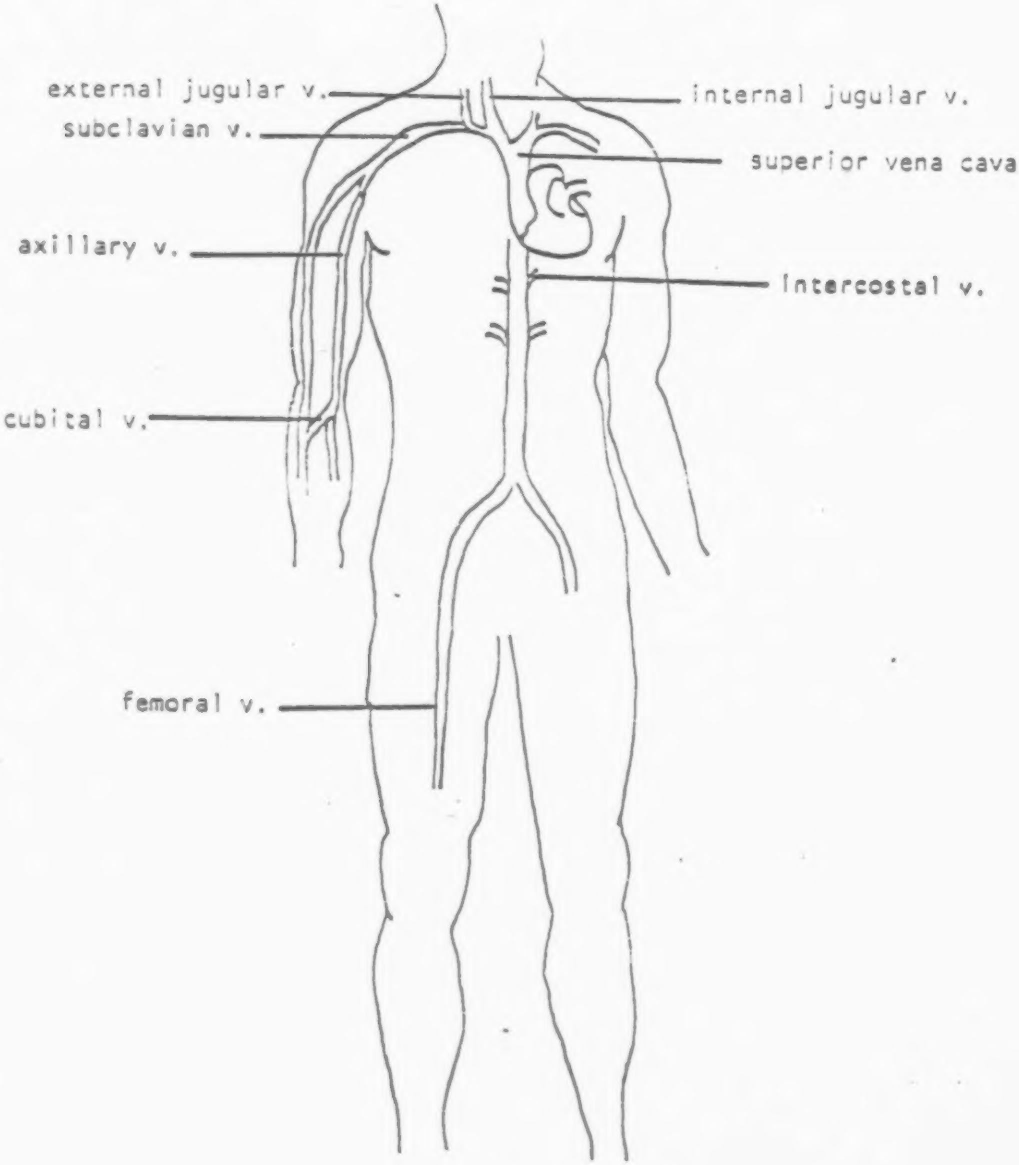


FIG. 7. EXTERNALIZED CATHETER THREADED THROUGH THE SUBCLAVIAN VEIN TO THE SUPERIOR VENA CAVA. THE CATHETER IS TUNNELLED UNDER THE SKIN BETWEEN THE EXIT SITE AND THE ACCESS VEIN.

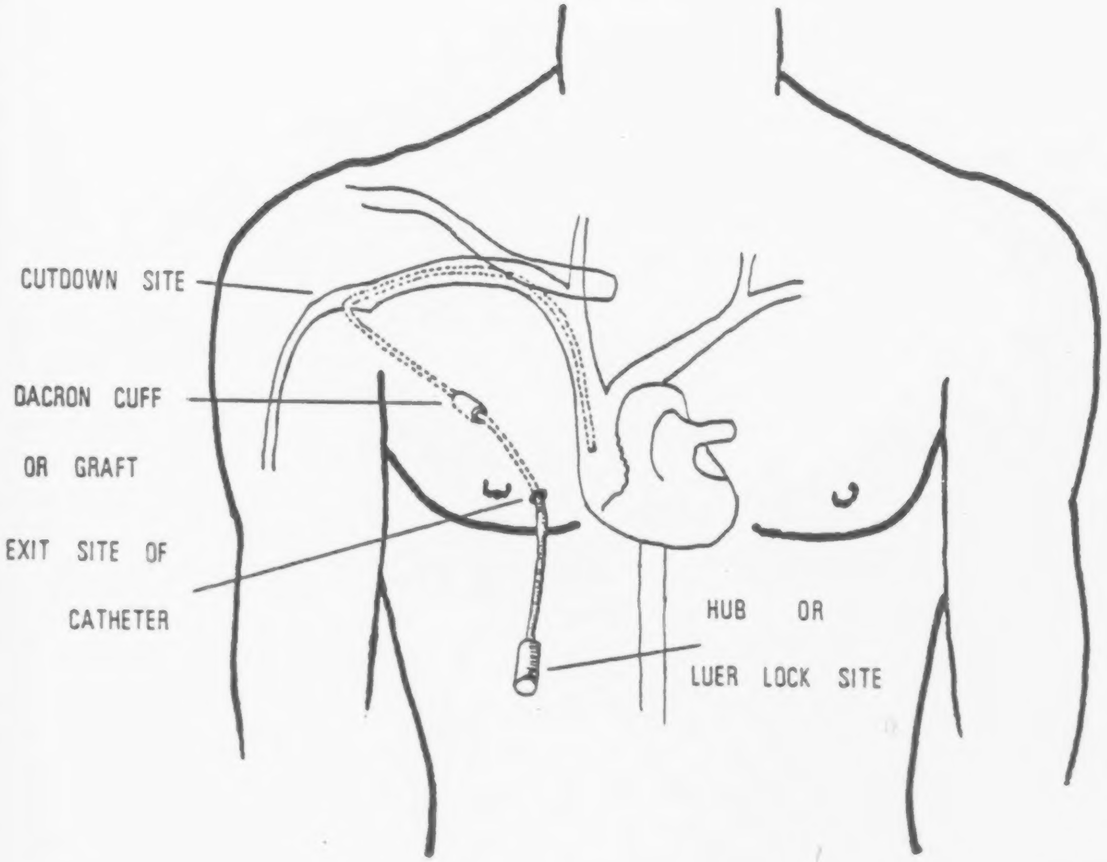


TABLE 1. Enteral Feeding Tubes

PLACEMENT TECHNIQUE	CLINICAL USES	POTENTIAL PROBLEMS
Nasogastric External measurement: nostril, ear to xiphisternum; placed by professional or with instruction, family member or patient; tube stiffened by ice water or a stylet; position tested by injecting air and auscultating air bubble passing through fluid or aspirating acid gastric contents.	Short-term clinical situations (a few wks.). Placement can be intermittent. Normal gastric emptying required. Bolus feeds or continuous drip.	Aspiration pneumonia from regurgitated stomach content; irritation of nasopharynx or esophogastric junction with bleeding and/or stricture.
Nasoduodenal or Nasojejunal External measurement: nostril, ear to anterior superior iliac spine in adults; to the medial malleolus in infants; weighted tube may pass spontaneously through pylorus if patient lies on right side; or placed with stiffening stylet under flouroscopy; position tested by aspirating alkaline duodenal contents or checking by x-ray.	Short-term clinical situations. Used if gastric emptying impaired or to infuse beyond a high bowel fistula such as an esophogeal tear, gastric or duodenal fistula.	Passing tube through pylorus; preventing the spontaneous pulling back into stomach; continuous drip required and tends to cause diarrhea; tubes stiffen with time; can lacerate pylorus or gastroesophogeal junction if pulled out rapidly.
Pharyngostomy/Esophagostomy Tube placed surgically through side of neck into pharynx.	Long-term access. No nasopharyngeal irritation; once tract established tubes can be replaced.	Aspiration if tube in stomach; pharyngeal scarring causes distortion of normal anatomy; causes swallowing difficulty.
Gastrostomy Tube placed through the abdominal wall into the stomach, either by a percutaneous endoscopic technique using local anaesthetic or surgically via an abdominal incision using a spinal or general anaesthetic.	Long-term access. Once tract is established tubes can be replaced; used where swallowing is impaired either because of mechanical obstruction or neurological discoordination.	Irritation around tube site; aspiration of regurgitated stomach contents; displacement of tube into peritoneal cavity or if held in situ by balloon; obstruction of the pylorus.

cont. on next page

TABLE I. Enteral Feeding Tubes (cont.)

PLACEMENT TECHNIQUE	CLINICAL USES	POTENTIAL PROBLEMS
Jejunostomy		
Tube placed surgically through abdominal wall into proximal loop of jejunum, tethered to anterior wall by suture; fine bore tube inserted by diagonal tract into bowel lumen or large bore with an anchoring suture.	Long-term access. Used for defective gastric emptying; fine bore tube recommended as postoperative backup where prolonged gastric atony may occur.	Irritation at tube exit site, especially large bore tube; clogging or displacement of tube continuous drip usually required; diarrhea common
Combined Gastrojejunostomy Tubes		
Tube placed surgically with jejunal arm thread beyond the pylorus.	Allows for simultaneous gastric suction and jejunal infusion; used where patient particularly at risk for aspiration of gastric contents.	Not yet widely available.

TABLE II. Enteral Feeding Formulas

CATEGORY	CLINICAL INDICATIONS	TUBE OF CHOICE	COMMENTS
Blenderized Formulas Mixture of pureed meat, fruit, vegetables, sometimes added nonfat dry milk, fiber, vitamins and minerals; highly viscous.	Normal digestion and absorption required; used with pharyngostomy, cervical esophagostomy or gastrostomy tubes.	Large bore 12-18 French	Lowest cost; 2 or more liters needed daily; bolus feed
Polymeric Formulas Mixture of whole proteins, polysaccharides and triglycerides; contains no fiber; lower viscosity than blenderized.	Normal digestion and absorption required; can be fed into esophagus, stomach, duodenum, or jejunum.	Small bore 8-10 French	2 or more liters needed daily; bolus, gravity, or pump
Monomeric Formulas Mixture of predigested protein, carbohydrate (CHO), and a small amount of triglyceride; contains no fiber; the lowest viscosity of all formulas.	Used for inflammatory bowel disease, chronic pancreatitis, GI fistula, radiation or chemotherapeutic enteritis, pan maldigestion, pan malabsorption or transition feeding from parenteral to enteral therapy.	Small bore 5-6 French	Higher cost than polymeric; 1.5-3 liters needed daily; pump
Disease-related Formulas Devised to meet the nutritional needs of specific disease states; varying amounts of protein, amino acid ratios, CHO and electrolytes; low viscosity	Used for renal failure, hepatic encephalopathy, stress, trauma and respiratory failure	Small bore 5-6 French	Highest cost 2 liters or more daily, gravity or pump
Modular Formulas Made-to-order feedings of individual constituents; viscosity depends on quantities of protein, CHO and fat used	Used for specific metabolic abnormalities, such as glycogen storage disease	varies, depends on viscosity	Higher cost than monomeric; 1.5 or more liters needed; bolus, gravity or pump

TABLE III. Parenteral Nutrition Catheters

TYPES OF CATHETERS

- A. Externalized
  - 1. single, double or triple lumen; 2nd and 3rd channels used for intravenous medications or blood drawing
- B. Subcutaneous port
  - 1. involves a small reservoir with an overlying rubber diaphram which is self sealing
  - 2. port must be entered by a J-shaped needle
  - 3. not all patients like the daily needle stick
  - 4. if line is not in use, the buried port makes showers and swimming less hazardous

CATHETER MATERIAL

- A. Polyvinylchloride, polyethylene, polyurethane or teflon
  - 1. Advantages
    - a. inherent stiffness allows easy threading into the vein
  - 2. Disadvantages
    - a. stiffness allows catheter to be in direct contact with vessel wall causing thrombosis
    - b. stiffness increases over time, causing kinks or fractures
- B. Silicone Rubber
  - 1. Advantages
    - a. very pliable, less kinking
    - b. less traumatic to vessel wall
    - c. inert; inducing little reaction or adherence
  - 2. Disadvantages
    - a. difficult to thread into vein
    - b. falls out more easily due to nonadherance
    - c. potential for tearing

SITES OF VENOUS ACCESS

- A. Distal tip of catheter best placed in mid-portion of superior vena cava.
- B. Enters venous system via:
  - 1. percutaneous stick into the subclavian, external jugular, or anterior cubital vein
  - 2. cut down site on external jugular (via common facial vein) femoral, axillary or intercostal vein
- C. All catheters can be tunnelled superficially to a distal site which:
  - 1. may provide a barrier to skin organisms infecting the line
  - 2. places exit site at convenient place for self care in patients going home

TABLE IV. Standard Total Parenteral Nutrition Solution (24 Hours) for a 70 kg Adult

Fluid	3 Liters
Protein (amino acids)	.2-.3 g nitrogen/kg
Calories*	25-40 kcal/kg
Essential fatty acids (lipids)	2% of total calories
Electrolytes	
Sodium	100 mEq
Potassium	100 mEq
Chloride	130 mEq
Acetate/gluconate	90 mEq
Calcium	15 mEq
Magnesium	20 mEq
Phosphorous	300 mg
Trace Elements	
Zinc	5 mg
Copper	1.5 mg
Iodine	120 ug
Selenium	100 ug
Chromium	15 ug
Manganese	2 mg
Vitamins	
Ascorbic acid	100 mg
Thiamine	3 mg
Riboflavin	3.6 mg
Niacin	40 mg
Pantothenic acid	15 mg
Pyridoxine	4 mg
Biotin	60 ug
Folic acid	400 ug
Cobalamin	5 ug
Vitamin A	4000 I.U.
Vitamin D	400 I.U.
Vitamin E	15 mg
Vitamin K	200 ug

*Provided prinicpally as dextrose.

TABLE V. Chronological Occurrence of Complications from Total Parenteral Nutrition

	First 48 Hours	First 2 Weeks	Three Months Onward
Mechanical	Complications from catheter insertion: cephalad displacement pneumothorax hemothorax Detachment of line at catheter hub with blood loss or air embolism	Catheter coming out of vein, more common if silastic Detachment of line at catheter hub with blood loss or air embolism	Detachment of line at catheter hub with blood loss or air embolism Fracture or tears in catheter
Metabolic	Hyperglycemia Hypophosphatemia Hypokalemia	Hyperosmolar nonketotic hyperglycemic coma Hyponatremia Hypomagnesemia Hypopotassemia Hypocalcemia Acid-base imbalance	Essential fatty acid deficiency Zinc, copper, chromium, selenium, molybdenum deficiency Iron deficiency Vitamin deficiency TPN metabolic bone disease TPN liver disease
Infectious		Catheter-induced sepsis	Catheter-induced sepsis Tunnel infections

APPENDIX A(1) ENTERAL FEEDING TUBES+

TUBE	COMPANY	COMPOSITION	FEATURES	PRICE++
ENTRIFLEX	Biosearch Medical Products	Polyurethane	Radiopaque tip Mercury weighted Stylet included 36, 43" long, 8 Fr*	18.00
DOBBHOFF		Polyurethane	Radiopaque tip Mercury weighted Uses Entriflex stylet 43" long, 8 Fr	19.00
KEOFEED	IVAC Corporation	Silicone	Radiopaque tip Tungsten weighted Stylet included 36, 42" long, 5-8 Fr	9.00
SURGIFEED JEJUNOSTOMY		Silicone	18" long, 5-8 Fr	22.00
DUO-TUBE	Argyle	Silicone	Radiopaque Mercury or silicone weighted 40" long, 5-8 Fr Thinner tubing so greater inside diameter for thicker formulas	ND**
VIVONEX	Norwich Eaton	Polyurethane	Radiopaque Tungsten weighted 45" long, 8 Fr	10.00
FLEXIFLO	Ross Laboratories	C-Flex	Radiopaque Tungsten weighted Teflon coated stylet 36,45" long, 8,12 Fr	12.50
TRAVASORB	Travenol Laboratories	Polyurethane	Radiopaque Tungsten weighted Prelubricated stylet 45" long, 8 Fr	16.25

+Informtion supplied by manufacturer.
++List prices do not, of course, reflect actual purchase prices that may include volume discounts, special contracts, or what is actually paid by the third party payers.
*Fr=French=0.33 cm. (a measure for the tube's outside diameter).
**ND=No Data (in the material available from the manufacturer the price was not included).

APPENDIX A(1) ENTERAL FEEDING TUBES+ (cont.)

TUBE	COMPANY	COMPOSITION	FEATURES	PRICE++
FLOW THRU SAFE-T-FLEX	Superior Plastic Products	Polyurethane	Radiopaque Silicone weighted 42" long, 9 Fr* graduated to 14 Fr Bolus tip	16.00
CONVENTIOAL SAFE-T-FLEX		Silicone	Radiopaque Bronze spring weighted Braided wire stylet 42 in. long 6, 8, 10 Fr.	13.00
MED-PRO	Vicra Corp.	Silastic	PVC outer stent	ND**
CORPAK	Corpak Co.	Polyurethane	Radiopaque Tungsten weighted Braided wire stylet 36, 43" long 6, 8, 10 Fr	9.00
KANGAROO	Chesebrough Ponds, Inc.	Polyurethane	Radiopaque stripe Tungsten weighted Braided wire stylet 43" long, 8 Fr	15.00

+Informtion supplied by manufacturer.

++List prices do not, of course, reflect actual purchase prices that may include volume discounts, special contracts, or what is actually paid by the third party payers.

*Fr=French=0.33cm. (a measure for the tube's outside diameter.)

**ND=No Data (in the material available from the manufacturer the price was not included).

APPENDIX A(2) ENTERAL FEEDING PUMPS+

PUMP*	MANUFACTURER	FLOW RATE	AUDIO/VISUAL ALARMS	WEIGHT & OTHER FEATURES	PRICE++
Dobbhoff	Biosearch Medical Prod.	1-300 ml/hr	No flow Low battery	4.75 lbs., handle for ambulatory use	495-525
Enteral #14-7005		5-300 ml/hr	No flow/occ. Rate change Low battery	4.5 lbs., 7-hr. battery operation	495-525
Kangaroo 220	Chesebrough-Ponds, Inc.	5-295 ml/hr	Occ/empty rate change low battery	4.2 lbs. With pole clamp & power converter	505-990**
Kangaroo 330		1-295 ml/hr	Occ/empty Low battery Hold alarm	5 lbs. 3-hr. battery	595-1090
Kangaroo 2 Home Care		5-295 ml/hr	Occ/empty Rate change Low battery	3.5 lbs., optional car lighter plug adapter	354-600 12.50
Corpak VTR 300	Corpak Company	1-299 ml/hr	Occ/empty Low battery	6.5 lbs. (with cord & pole clamp)	275-300
IVAC #3000 Keofeed	IVAC Corporation	1-300 ml/hr	Low battery Rate change	Portable [Bag and pump set]	595
Flexiflo	Ross Laboratories	50-200 ml/hr	None		305
Flexiflo-II		20-250 ml/hr	Occ/empty Low battery	Portable 8-hr. battery	550
Superior Enteral Pump	Superior Healthcare Group, Inc.	10-390 ml/hr	Occ/empty Rate change Low battery	Can be used on Table or IV stand Takes most tubing	ND***
Enteral Delivery Pump #430	IMED Corporation	1-299 ml/hr	Rate change Occ/empty Low battery	7.6 lbs. 8 hr battery Table or IV stand	650
Flo-gard 2000	Travenol Laboratories	5-300 ml/hr	No flow Occ/empty Rate change Low battery	7 lbs. Portable	595

+Information supplied by manufacturer.

*Pumps run on AC current or can be used for short periods, 1-3 hours, on rechargable battery generally included with pump.

++Price ranges reflect discounts for quantity purchases, contracts, etc. Pumps can also be rented on a monthly basis.

**Price range reflects large contract prices for institutions to indivdual patient purchases for long-term home use.

***ND=No Data (in the material available from the manufacturer the price was not included).

APPENDIX A(2) ENTERAL FEEDING CONTAINERS+

CONTAINER	COMPANY	MATERIAL	FEATURES	PRICE++
DOBBHOFF	Biosearch Medical Products	Vinyl Bag	Size: 1 liter 3 holes for hanging Universal outlet Disposable Includes pump set	4.12- 5.65
KEOFEED	IVAC Corporation	Vinyl Bag	Size: .5 or 1.5 liter Delivery set avail. 1 hole for hanging Zip lock top Universal outlet Use with pump or drip	2.52- 3.10
VIVONEX	Norwich Eaton	Bag	Size: 1 liter 1 hole for hanging Side snap cap Universal outlet Disposable	4.80
FLEXIFLO TOP-FILL	Ross Laboratories	Bag	Use with pump or drip Size: 1 liter 1 hole for hanging Side screw on cap Universal outlet Disposable With pump set	2.92 6.10
FLEXITAINER		Plastic Bottle	Use with pump or drip Size: .5, 1 liter 1 hole for hanging Self collapsing Disposable	2.75
SAFE-T-FLEX	Superior Plastic Products	Plastic Bottle	Use with pump or drip Size: .75, 1 liter 1 hole for hanging Top screw on cap Universal outlet Self collapsing Reusable	2.25

+Information supplied by manufacturer.

++List prices do not, of course, reflect actual purchase prices that may include volume discounts, special contracts, or what is actually paid by the third party payers.

*ND=No Data (in the material available from the manufacturer the price was not included).

APPENDIX A(2) ENTERAL FEEDING CONTAINERS+ (cont.)

CONTAINER	COMPANY	MATERIAL	FEATURES		PRICE++
EVA	Gil-Med Industries	Ethyl vinyl Acetate	Use with pump or drip		
			Size: 1, 3 liter		
			Top clamp	1 L	7.30
				3 L	7.95
CORPAK	Corpak Co.	Bag	Size: 1 liter		
			Roberts valve flip top		
			1 hole for hanging		
			2 outlet ports		
			Admin. set available		5.00
TRAVASORB	Travenol Laboratories	Bag Tapered	Size: 1.3 liter		
			Top fill, preattached cap, rigid neck		
			1 hole for hanging		
			2 outlet ports		3.75
			With admin. set		4.60
			With pump set		5.25
KANGAROO	Chesebrough Ponds, Inc.	Bag	Size: .5, 1, 1.2, 1.6 liter		
			Easy cap closure		
			1 outlet port		
			includes pump set		
			Without ice pouch		5.63-7.00
			With ice pouch (1 or 1.2 liter only)		5.11-5.88

+Information supplied by manufacturer.

++List prices do not, of course, reflect actual purchase prices that may include volume discounts, special contracts, or what is actually paid by the third party payers.

*ND=No Data (in the material available from the manufacturer the price was not included).

APPENDIX A(3) COMMERCIAL ENTERAL FORMULAS

PRODUCT	COMPANY	PRICE/LITER
Blenderized Formulas		
VITANEED	BIOSEARCH	6.19
COMPLEAT-B	SANDOZ	7.36
COMPLEAT MODIFIED FORMULA		8.26
NUTRI-1000	CUTTER	ND*
FORMULA-2		ND*
Polymeric Formulas		
ISOCAL-HCN	MEAD JOHNSON	5.62
SUSTAGEN		7.00
SUSTACAL		4.17
ISOCAL		4.17
SUSTAGEN-HC		5.40
LONALAC		4.56
PORTAGEN		4.50
TWO CAL HN	ROSS	3.98
ENSURE PLUS		2.90
ENSURE PLUS HN		3.19
ENSURE		2.53
ENSURE HN		2.10
ENRICH		3.60
OSMOLITE HN		2.22
OSMOLITE		2.02
TRAVASORB	TRAVENOL	2.31
MAGNACAL	BIOSEARCH	5.78
ENTRITION		5.17
RENU		3.50
RESOURCE CRYSTALS	SANDOZ	2.45
MERITENE		3.69
CITROTEIN POWDER		3.82
ISOTEIN HN		16.60

*ND=No Data (in the material available from the manufacturer the price was not included).

APPENDIX A(3) COMMERCIAL ENTERAL FORMULAS (cont.)

PRODUCT	COMPANY	PRICE/LITER
Monomeric Formulas		
VIVONEX	NORWICH EATON	5.46
VIVONEX-HN		13.60
PRECISION-LR	SANDOZ	7.36
PRECISION ISOTONIC		9.42
PRECISION-HN		14.01
CRITICARE	MEAD JOHNSON	16.70
VITAL	ROSS	21.36
SLD		4.17
TRAVASORB STD	TRAVENOL	6.86
TRAVASORB MCT		11.84
TRAVASORB-HN		12.50
VIVEP	CUTTER	ND*
Modular Formulas		
Protein: Powder form, reconsitituted with water		
PROPAC	BIOSEARCH	4.15/100 gms
CASEC	MEAD JOHNSON	9.00/100 gms
RDP	NAVACO	4.75/100 gms
NUTRISOURCE PROTEIN	SANDOZ	5.68/100 gms
Carbohydrate (CHO):		
SUMACAL POWDER	BIOSEARCH	.69/100 gms
PURE CHO POWDER	NAVACO	.82/100 gms
LIQUID CHO	NAVACO	8.75
HYCAL	BEECHAM	ND*
CAL-POWER	GM	ND*
POLYCOSE LIQUID	ROSS	7.15
MODUCAL POWDER	MEAD JOHNSON	1.15/100 gms
NUTRISOURCE LIQUID CHO	SANDOZ	7.66

*ND=No Data (in the material available from the manufacturer the price was not included).

APPENDIX A(3) COMMERCIAL ENTERAL FORMULAS (cont.)

PRODUCT	COMPANY	PRICE/LITER
Modular Formulas (cont.)		
Fat:		
HIGH FAT POWDER	NAVACO	1.76/100 gms
MICROLIPID	BIOSEARCH	15.12
MCT OIL	MEAD JOHNSON	27.00
NUTRISOURCE MCT	SANDOZ	7.00
Disease-Related Formulas		
HEPATIC AID	MCGAW	ND*
AMIN-AID		ND*
TRAVASORB RENAL	TRAVENOL	22.80
TRAVASORB HEPATIC		43.20
PULMOCARE	ROSS	3.98
STRESSTEIN	SANDOZ	25.06
TRAUMACAL	MEAD JOHNSON	7.08
T.E.N.	NORWICH EATON	21.34

*ND=No Data (in the material available from the manufacturer the price was not included).

APPENDIX B(1) PARENTERAL FEEDING CATHETERS* [illegible]

CATHETER	MANUFACTURER	COMPOSITION	FEATURES	PRICE
BROVIAC	Everted	Silicone Rubber	90cm long, 1.0mmOD** Dacron cuff Barium impregnated Luer lock connector Teflon reinforced exterior portion	36.00
PEDIATRIC BROVIAC		Silicone Rubber	71cm long .9mm(3Fr)or 1.4mm(4Fr)OD	49.00
REPAIR KIT			....	45.00
HICKMAN		Silicone Rubber	90cm long 3.2mmOD Dacron cuff	
			1cuff, radiopaque	37.00
			2cuff, clear	39.00
DUEL LUMEN HICKMAN			90cm long 2.2mm, 3.2mmOD radiopaque Dacron cuff	50.00
REPAIR KIT			....	36.00
COOK	Cook, Inc.	Silicone Rubber	Radiopaque Dacron cuff 90cm long, 7,10Fr OD	31.50
DUEL LUMEN COOK			90cm long, 12 Fr OD	43.50
PEDIATRIC COOK			65cm long, 4Fr OD	
			............1 lumen	41.50
			............2 lumen	53.50
COOK CATHETER KIT			Includes wire guide, introducer needle, peel away sheath, and catheter	
			............1 lumen	45.50
			............2 lumen	55.50
REPAIR KIT			............1 lumen	32.50
			............2 lumen	38.50

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*Information supplied by manufacturer. List prices do not reflect actual purchase prices that may include volume discounts, special contracts, etc.
**OD=Outer Diameter

APPENDIX B(1) PARENTERAL FEEDING CATHETERS (cont.)

CATHETER	MANUFACTURER	COMPOSITION	FEATURES	PRICE
SCRIBNER TYPE	Extracorporeal	Silicone Rubber	39cm long 1mmID* Radiopqaque Dacron cuff	[1977] 30.00
TRIPLE LUMEN	Arrow International	Poly-urethane	20,30cm long 16,18,18guage lumens Color coded hubs	180.00
INFUSE A PORT	Infusaid Corp.	Polyether sulfone plastic Silicone Rubber	Base-4.7cm Port ht-1.58cm 50.8cm long 2.3mmOD Radiopaque Wt-12.1gms Uses Infusaid or Huber needles	250.00
MEDIPORT	Cormed	Stainless steel +dacron/silicone rubber	Base-36mm Ht-1.4cm 50cm long Radiopaque Wt-20gms Uses huber needles 2 or 3mmOD	325.00
DUAL LUMEN DUAL SEPTUM MEDIPORT		Same	Base-35.5mm Ht-14mm Wt-45gms OD-4mm(12Fr) 50cm long	475.00
CORCATH		Silastic Elastomer	Dacron cuff Latex oversheath Luer lock Radiopaque	
			1)2.1mm(6Fr)OD 84cm long	35.00
			2)3.0mm(9Fr)OD 90cm long	37.00
			3)1.5mm(4Fr)OD 72cm long	45.00
			4)Duel Lumen 4mm(12Fr)OD 91.5cm long color coded hubs	48.00
REPAIR KITS			....	40.00

*ID=Inner Diameter

APPENDIX B(1) PARENTERAL FEEDING CATHETERS (cont.)

CATHETER	MANUFACTURER	COMPOSITION	FEATURES	PRICE
HEMED	Gish Biomedical	Silicone Rubber	Luer lock, radiopaque Dacron cuff 5 sizes	US$-
			..........1 lumen	38-48.00
			..........2 lumen	52.00
CATHETER INTRODUCER			For placement of catheter	25.50
CATHETER KIT			Introducer, Tunneller Catheter	
			..........1 lumen	69-79.50
			..........2 lumen	83.50
REPAIR KIT			..........1 lumen	30.00
			..........2 lumen	ND*
PORTACATH	Pharmacia Nu Tech	Stainless steel port Silastic catheter	Base-24mm, Ht-13mm 2 catheter sizes: 2,2.8mm OD Uses huber needles	330.00
QUINTON RAAF DOUBLE LUMEN	Quinton Instrument	Silicone Rubber	84cm long, 4.5mmOD Dacron cuff Color coded lumens Radiopaque	55.00
SINGLE LUMEN		Silicone Rubber	89cm long Radiopaque Dacron cuff 2 lumen sizes	35.00
PEDIATRIC SINGLE LUMEN		Silicone Rubber	78cm long 1.3mmOD	45.00
REPAIR KIT			....	60.00

*ND=No Data (in the material available from the manufacturer the price was not included).

APPENDIX B(2) PARENTERAL INFUSION PUMPS+

09.01

PUMP*	MANUFACTURER	FLOW RATE	AUDIO/VISUAL ALARMS	WEIGHT & OTHER FEATURES	PRICE++
LifeCare Model 4	Abbott Laboratories	1-999 ml/hr	Occlusion Dose complete Dose limit Air in line KVO* Low battery	13 lbs., 6-hr. battery at 50 ml/hr.; cassette type	2,900
Cormed II Ambulatory ML 6-8 (includes 2 rechargable power packs, plug in flow rate meter & power pack charger)	Cormed, Inc.	600-3000ml/ 24 hrs.	Low battery Low flow High flow Elec. prob.	17 oz.; 48-hr. 5V rechargable battery;	1,425
				Vest-type support harness	150
				Administra. set	6
				Extension set	5
IMED #927, 928, 929	IMED Corporation	range: 1-299to 1-1599 ml/hr	No data	13 lbs.	range: 2,600-3,950
IVAC #560, 565	IVAC Corporation	1-999 .1-99.9 ml/hr respectively	Low battery Low flow Occlusion	14 lbs.	2,795
Sigma 6000	SIGMA	.1-999 ml/hr	Air/occ. Low battery KVO, high/ low rate,	10.2 lbs., separate piggyback settings 4-hr. battery	2,495
Infutrol 6000	Valleylab, Inc.	1-499 ml/hr	Cassette not in; Air/occ. Low battery System fail. KVO	9.2 lbs., 10-hr. batt. life at 99.9 ml/hr	1,895
				Admin. set	7.45
Infutrol 7000		.1-699.9 ml/hr	Above plus KVO off	11 lbs., 7-hr. battery ,pt. occ. monitor	2,495

+Information supplied by manufacturer.

*Pumps run on AC current or can be used on rechargable battery generally included with pump. In addition to pump an IV pole is required and several "disposables" -- a filter, an IV administration set and casette, and an extension set of tubing so patient can have some freedom of movement (particularly important if sleeping).

++List prices do not, of course, reflect actual purchase prices that may include volume discounts, special contracts, or what is allowed and actually paid by third party payers. Pumps can also be rented on a monthly basis.

**KVO=Keep Vein Open.

APPENDIX B(3) PARENTERAL SOLUTIONS*

SOLUTIONS	COMPANY	PRICE
DEXTROSE	TRAVENOL	[1984]
	10-70%.....1L.......glass	8.52-18.66
	....................Viaflex	9.36-17.74
	5% w/.9%NaCl 1L	5.42
	10% w/.9%NaCl	6.17
	5% w/RINGERS	6.16
	5% w/LYTES	7.68
	5% w/ 40mEq KCl	7.46
	ABBOTT	
	10-70% part fill(500ml/1)	5.77-14.85
	50%.......1L........glass	14.33
	...................plastic	17.54
	70%.......1L........glass	17.82
	...................plastic	21.80
	5% w/ .9% NaCl	5.49
	5% w/ LACTATED RINGERS	6.18
	IONOSOL-10% w/LYTES	8.72
	5% w/40mEq KCl	7.12
	AMERICAN MCGAW	[12/84]
	5,10,20,50%............500ml	5.51
	5% w/20,40mEq KCl.........1L	7.75
	5% w/.9% NaCl.............1L	5.97
	10% " " 1L	6.85
	5% w/.45% NaCl,40mEqKCl...1L	7.75
	Lactated Ringers..........1L	6.21
	.................w/5% dex	6.74
	Ringers...................1L	6.19
AMINO ACIDS	**TRAVENOL**	[1984]
	TRAVASOL..................1L	
	5.5% AMINO ACIDS w/ LYTES	50.02
	8.5%....................	66.00
	10%.....................	74.70
	8.5% TRAVASOL KIT incl. 50% dex-500ml/1000ml transfer set, additive cap	
	.................w/ LYTES	47.69
	................w/o LYTES	44.69
	ABBOTT	
	AMINOSYN..................1L	
	3.5% AMINO ACIDS w/LYTES	25.33
	8.5%..................(1/2L)	33.57
	8.5% AMINO ACIDS,NO LYTES	63.94
	10%..................	72.95
	AMERICAN MCGAW	
	Freamine III Kit 8.5%,1/2L freamine, 1L w/ 500ml 5% dex, trans set, add. cap	46.71
	Freamine III	
	8.5%.................1L	68.43
	10%..................1L	78.07
	Procalamine	
	3% AA, 3% glycerin w/LYTES..1L	30.47

*Information supplied by manufacturer.

APPENDIX B(3) PARENTERAL SOLUTIONS (cont.)

FAT EMULSIONS	**TRAVENOL**	[1984]
	TRAVAMULSION.........500ml	32.36
	ABBOTT	
	LIPOSYN	
	10% SAFFLOWER, 1.2% EGG PHOSPH ATIDES, 2.5% GLYCERIN IN H2O	
	10%................500ml	30.78
	20%................500ml	46.11
	KABIVITRUM	
	INTRALIPID 10%	ND*
	10% soybean......250,500ml	
	AMERICAN MCGAW	
	IV FAT	
	10%..................500ml	30.75
	20%..................250ml	28.47
TRACE ELEMENTS	**AMERICAN QUININE**	
	MTE.....................10ml	
	Zn1mg,Cu.4mg,Cr4mcg,Mn.1mg/ml	6.60
	MTE CONCENTRATE 10ml	
	Zn5mg,Cu1mg,Cr10mcg,Mn.5mg/ml	9.60
	PEDIATRIC MTE 10ml	
	Zn.5mg,Cu.1mg,Cr1mcg,Mn.03mg/ml	7.60
	ZINC SULFATE	
	5mg/ml.................5ml	2.80
	1mg/ml................10ml	1.12
	TRAVENOL	[1984]
	MTE.....................3ml	2.02
	.......................10ml	5.94
	ZINC 1mg/ml............10ml	1.84
	ABBOTT	
	MULTIPLE TRACE METALS	
	Zn4mg,Mn.8mg,Cu1mg,Cr10mcg 5ml	2.14
	AMERICAN MCGAW	
	MULTIPLE TRACE ELEMENTS	
	Zn1mg, Cu.4mg, Mn.1mg, Cr4mcg	
	.......................10ml	5.94
	ZINC SULFATE 1mg/ml.....10ml	1.89
	LYPHOMED	
	MTE-2 (Zn1mg,Cu.4mg)....10ml	3.30
	MTE-3 (+Cr4mcg).........10ml	4.40
	MTE-4 (+Mn.5mg).........10ml	5.50
	MTE-5 (+Se60mcg)........10ml	12.75
	MTE-6 (+Iodine75mg).....10ml	14.86
	Neotrace 4..............2ml	4.32
	PTE-4 (sl higher).......10ml	11.45
	ZINC SULFATE	
	5mg/ml..............10ml	6.86
	1mg/ml..............10ml	1.45

*ND=No Data (in the material supplied by the manufacturer the price was not included).

APPENDIX B(3) PARENTERAL SOLUTIONS (cont.) 019_04

	ARMOUR PHARMACEUTICALS	
	MULTITRACE	
	MULTITRACE CONC.	
	MULTITRACE PED	
	MULTITRACE - 5	ND*
ELECTROLYTES	**AMERICAN QUININE**	
	POT CHLORIDE.......20 mEq/10ml	4.00
	....................40 mEq/20ml	5.70
	CA GLUC.....10%(.465 mEq/ml)10ml	5.00
	MAG SULFATE...50%(500mg/ml)2ml	2.40
	LYPHOMED	
	CA GLUC.10%...............10ml	.75
	LYPHOLYTE-mult. lytes.....20ml	4.70
	MAG SULFATE 50%............2ml	.42
	POT CHLORIDE........40mEq/20ml	.52
	TRACELYTE	
	lytes/trace elements......20ml	8.70
VITAMINS	ARMOUR PHARMACEUTICALS	
	MVI-12 2-5ml vials	ND*
	MVI-12 LYOPHILIZED	
	reconstitute with 5ml water	
	MVI-PEDIATRIC 10ml	ND*
	MVI	
	higher formulation for 9	
	vitamins 10ml	ND*
	ROCHE	
	SYNKAVITE	
	Synthetic H20 soluble Vit K	
	analog..............5mg/ml-1ml	
	...................10mg/ml-1ml	
	...................75mg/ml-2ml	ND*
SPECIAL FORMULAS	**AMERICAN MCGAW**	
	6.9% FREAMINE-HBC	
	45% BCAA (12:1 BCAA:AA ratio)	
	for trauma, sepsis..750ml/1000ml	54.50
	8.0% HEPATAMINE	
	36% BCAA (37:1 BCAA:AA ratio)	
	for liver disease..........500ml	62.50
	5.4% NEPHRAMINE	
	for renal disease..........250ml	41.59
	TRAVENOL	
	RENAMIN	
	for renal disease..........250ml	39.38

*ND=No Data (in the materials available by the manufacturer the price was not included).

TASK 2. UTILIZATION OF NUTRITION SUPPORT (NS) IN THE UNIVERSITY TEACHING HOSPITAL

From February to June of 1984, a sex and age stratified random sample of inpatients age 65 and over was studied at the 725-bed Albany Medical Center Hospital, the principle teaching hospital of Albany Medical College, Union University. Data was collected on 96 subjects, 64 women and 32 men. Twenty-five percent (24) of these patients received tube delivered enteral feeding or intravenous (IV) nutrient solutions* or both. Specifically this included:

71% (17) tube feeding only
17% (4) tube feeding and IV nutrient solution
12% (3) IV nutrient solution only

Characteristics of the Patients Who Received Nutrition Support

There was no evidence that NS was determined by payment status for:

67 had Medicare only or Medicare plus private insurance
    and of this group, 16 (24%) received NS
28 had Medicaid or were Medicaid eligible
    and of these, 8 (29%) received NS

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*The IV support included peripheral and central line infusions. In general, peripheral infusions can only be done for a short term and the intravenous solutions must be of low concentration. However, central vein infusion can be done indefinitely and the solution can be more concentrated (see Task 1, Parenteral Techniques).

There was a trend toward decreased utilization with age:

Age 65-69 -- 29 (31%) received NS
70-74 -- 19 (21%) received NS
75+ -- 48 (21%) received NS

However this trend was not statistically significant.

The 96 patients were evaluated on 4 different functional rating scales from the Functional Assessment Inventory (FAI).[1] As can be seen in Figure 1 the social resources of those receiving NS and those not receiving NS were rated to be similar; however mental health, physical health, and the activities of daily living, a scale which measures the ability to live independently -- all showed greater impairment among those receiving NS as compared to those who did not. (A FAI economic assessment of these patients was not done because of concern about confidentiality.)

The diagnoses in the 24 patients receiving NS were:

11 (46%) -- central nervous system damage
    7 -- cerebrovascular accidents
    1 -- brain hemorrhage due to head injury
    1 -- spinal cord injury
    2 -- brain tumors
5 (21%)-- carcinomas with local or metastic bowel involvement
8 (33%) -- complex medical (4) or surgical (4) conditions

In comparison only 4 (5.6%) of the 72 who received no NS had central nervous system damage (2 had cerebrovascular accidents, 1 had Parkinson's disease and 1 had a brain tumor). Fifteen (21%) had carcinomas of various types. Diagnoses that appeared markedly more prevelant among this group than the NS receivers were heart and respiratory diseases and mental disorders.

Impact of the Nutrition Support

In 61 of these 96 patients, anthropometric studies were done allowing us to calculate a body mass index (BMI)[2] which is thought to be the single best measurement for determing desirable weight (weight in kg/height in cms^2). Of the 15 patients receiving nutritional support in this sample of 61, 1/3 were within the normal BMI range, 1/3 were above and 1/3 were below. Thus only 1/3 of the group receiving NS were malnourished as determined by BMI. In the 46 patients not receiving support, most (56%) were within the normal range and just 11% were malnourished. Since nutritional assessment was done once and not at the onset and conclusion of NS, this descriptive study cannot determine if there was any benefit from the therapy as demonstrated by improvement in body composition.

Half of the 24 patients who received NS died within one year of the study. Their average survival time from the beginning of their hospitalizations (which did not necessarily coincide with the beginning of the study) was 184 days (±SE 39) and ranged from 11 to 530 days.

A breakdown of the amount of nutrient support ordered for 22 of these 24 patients indicated that 45% were prescribed more than 1500 calories of nutrient support via tube or central vein. The remainder were prescribed less than 1500 calories via tube or peripheral vein. Specifically, the patients' records indicated:

41% (9) prescribed <1500 calories via tube
9% (2) prescribed <1500 calories via tube and peripheral IV
5% (1) prescribed <1500 calories via peripheral IV
27% (6) prescribed >1500 calories via tube
9% (2) prescribed >1500 calories via tube and central IV
9% (2) prescribed >1500 calories via central IV

Length of Stay and Outcome

Hospital stays for these 96 patients had a bimodal distribution with a cutoff between the curves at about 40 days. Looking at the patients in terms of long and short hospital stays shows:

Short stay (40 days or less):
No NS -- 42 (58%) average stay 17±1 day
NS -- 4 (17%) average stay 26±4 days

Long stay (41 days or more):
No NS -- 30 (42%) range 41-730
NS -- 20 (83%) range 41-772

These differences are highly significant ($p<0.002$) and like the functional ratings point to the fact that patients who received NS were in general sicker. None of these patients were discharged on nutrition support. One tube fed patient had been in the hospital for 722 days at the time of study, reflecting the frequent difficulty in New York State of transferring a patient with extreme need for physical care from an acute to a chronic health facility.

Outcome for the nutritionally supported looked as follows:

14 (58%) were discharged home
6 (25%) died in the hospital
4 (17%) were discharged to a nursing home

Of those 18 who left the hospital, 5 (27%) had at least one further hospitalization and 6 (30%) died during the one year follow-up period.

Discharge data was avialable for 54 of those not receiveing NS. Of this group:

39 (72%) were discharged home
9 (17%) were discharged to a nursing home
4 (7%) were discharged to another hospital
2 (4%) were discharged to a hospice

During the follow-up period, of those 50 who left an acute care setting, 23 (43%) had at least one more hospitalization and 7 (14%) died.

Indications for or Against the Use of NS in Elderly Patients

In general the indications for use of NS in the hospitalized elderly are the same as for younger patients and can be summarized as follows:

1. Evidence that the patient is malnourished or is at risk for developing malnutrition and cannot be restored or sustained by simpler oral feeding approaches.

2. Evidence that the patient would benefit physically and/or psychosocially from aggressive nutritional support.

In other words it should be possible to demonstrate that the patient stands to benefit from this expensive intervention and it is not an excercise in futility. On occasion benefit is not easy to gauge at the outset and NS is begun to prevent worsening of the prognosis until the clinical picture is clearer to the patient, their family and the health team. At the point that outcome can be assessed it may be appropriate to "back off" from NS, if the benefit is perceived by all involved to be negligible. Cost is never, in our experience, a determining factor.

What does happen, particularly with tube enteral feeding, is that it can switch from being a treatment that is medically indicated for rehabilitation to being baseline support or a hygienic measure. In the terminally ill bed-ridden patient it helps prevent bed sores and by maintaining immune function prevents intercurrent infections. Since an intercurrent infection may be the "natural" event leading to death in severely ill patients, the concept of "preventing" such an outcome is a difficult ethical decision which probably should be a reflection of the patients and their families wishes on a broad societal basis. It is not truly a physician decision.

From the data currently available from this university hospital study it seems likely that:

1) NS was instituted in the more chronically debilitated, sicker patients.

2) The NS may have been used in a variety of illnesses where nutritional intake was at least acutely a problem, rather than

the more specific gastrointestinal disorders characteristic of long-term NS in home patients. Presumably in such far-reaching treatment decisions there is a more precise definition of clinical benefit.

3) NS via a central line was a more certain medical decision that was done with planning and follow through, whereas tube feeding and peripheral IV feeding was more often token (under 1500 calories).

This study did not clarify whether the nutritional support truly influenced outcome.

Alternatives to NS

Encouraging the patient to eat a general or modified (full liquids, mechanically soft) diet is usually tried before resorting to parenteral or enteral feedings. Often the help of family or friends is elicited, especially if hand feeding is necessary or home cooked food is more appealing to the patient. Obviously this approach breaks down if there are no family available, for hand feeding is highly labor intensive and can easily fail because of staffing shortages. Staffing limitations may therefore dictate the introduction of tube feedings or even peripheral vein NS. It is unlikely that staffing considerations determine the more major decision of initiating central vein feeding, except in so far as this can only be safely undertaken in some areas of the hospital and moving the patient to such a location may depend on availability of beds and trained staff.

Consent

The need for consent of the patient does vary according to the method of feeding used. Nasogastric feeding generally requires only tacet consent. Intravenous lines placed in limbs similarly require only tacet consent and can accommodate nutrient solutions of low concentration. Central lines and total parenteral nutrition does require written consent of the patient, next of kin, or legal guardian, as does surgical placement of a gastrostomy or jejunostomy feeding tube.

Supply and Equipment Storage

The supplies, equipment and storage requirements related to nutritional support do not present any special procedures beyond the customary hospital rules and protocols.

At the Albany Medical Center Hospital parenteral solutions are stored in the pharmacy. Typically they are mixed according to a patient-specific formula by the pharmacist on a daily basis under appropriate procedures in the pharmacy IV area, transported to the floor, and stored in a refrigerator and administered by nursing staff during that 24-hour period. Tubing and cassettes are stored on the floor with additional stock stored in the pharmacy (tubing) or central supply (cassettes). Pumps are stored in central supply and ordered by the floor as needed. Occasionally there are spot shortages of pumps as they are used for infusing other solutions or are not returned to central supply but kept by floor personnel to make sure a pump is available if needed. In some institutions IV controllers (devices that control number of drops) are used to regulate the infusions when volumetric pumps are not available.

Enteral formulas are treated more as food and stored in a kitchen on the floor. Formulas that come ready to use from the can are opened and administered by nursing staff. Those that need to be mixed are prepared on a daily basis by hospital dietary staff in clean, disposable containers and then transferred into the enteral feeding containers by nursing staff. Both the canned and powdered enteral products need to be monitored for shelf life. Enteral pumps are ordered from central supply and in the Albany Medical Center Hospital the supply seems sufficient to cover the demand.

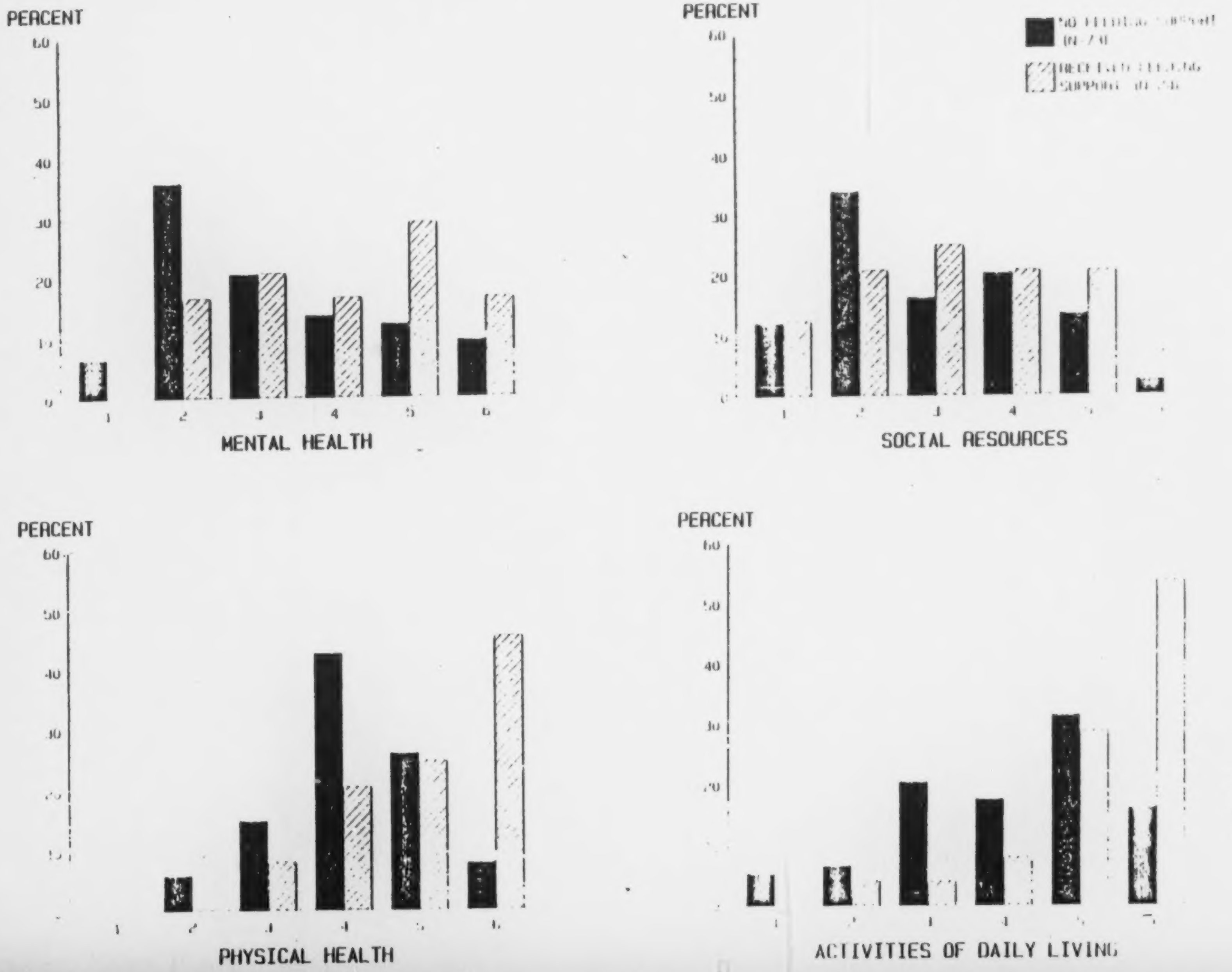
Notes

1. Pfeiffer E, Johnson T, Chiofolo, R: Functional assessment of elderly subjects in four service settings. J Am Ger Soc 29:433-437, 1981.

2. Thomas AE, McKay DA, Cutlip MB: Monograph for body mass indes (kg/m^2). Am J Clin Nutr 29:304, 1976.

Fig. 1. Functional Status Rating Scale Scores of Patients Receiving and Not Receiving NS

Scale: 1=Excellent, 2=Good, 3=Mildly Impaired, 4=Moderately Impaired, 5=Severely Impaired, 6=Totally Disabled



TASK 3. UTILIZATION IN THE NURSING HOME

Systematic data regarding use of enteral feeding supplements and intravenous nutritional support in nursing homes are unavailable. However, information from a single 200-bed skilled nursing facility will be presented here along with the nutrition support results from a systematic study of nurses attitudes toward use of this and other medical interventions.

Currently, 7 of 200 patients of the Daughters of Sarah Nursing Home in Albany, New York are receiving gastrostomy or jejunostomy feeding. None are receiving intravenous nutritional support or continuous hydration. Two of the patients are young women, ages 52 and 57, who have severe multiple sclerosis, one of whom is within and the other above a calculated ideal body weight range (based on figures from Master et al).[1] The other 5 individuals are between 77 and 91 years of age with severe dementing illness, tubes having been placed at the time of acute hospitalizations for strokes, septicemia, and in one case surgical removal of meningioma.

In the last year, one of the authors (M. Wolff) is aware of 4 cases where the family of a severely demented individual declined to consent to the placement of a feeding gastrostomy. In all cases, the family consulted a clergyman as well as health care professionals before deciding against tube placement. The legal and ethical questions regarding nutritional support were reviewed in a series of three articles in the Archives of

Internal Medicine.[2-4] Opinion generally divides based on whether artificial feeding is considered a medical intervention, analogous to medication use, or a custodial duty, analogous to the provision of basic hygienic conditions. In the former argument, futile treatment may be withheld or withdrawn. In the latter, basic sustenance must always be provided regardless of prognostic or quality of life considerations.

A revealing survey was completed at the Daughters of Sarah Nursing Home (see Appendix A) by Wolff et al. Head nurses of the facility were asked to complete questionnaires regarding which medical interventions they considered too aggressive for 100 of the 200 patients. Questionnaires were returned for 98 patients. Similar questions were asked regarding 20 patients who had died in the prior year. The data pertinent to this report are displayed in Table I. The nurses considered intravenous therapy too aggressive in 42% of the current residents, increasing to 47% if these residents were hypothetically to become immobile and to 66% if they were hypothetically to become comatose. Nasogastric feeding was less frequently considered inappropriate: 31% of current residents, 32% if permanently immobile, 46% if comotose. Basic nasogastric hydration was considered inappropriate only rarely: 11% of current residents, 11% if permanantly immobile, 22% if permantly comotose. Although tube feeding is often given via permanent gastrostomy or jejunostomy tubes, the figures for nasogastic feeding would probably be comparable with some positive bias toward use of the treatment.

Looking in detail at 11 patients whom the nurses would not wish to give even nasogastric hydration and 3 others in the group of deceased patients, all had chronic neurological failure. The most common feature was the perception by nurses that these individuals were depressed (12 of 14, 86%). Hence, a quality-of-life based preference was being enunciated by the nurses. It is interesting, and important from a governmental perspective, that if these findings are extrapolated to this nursing home's entire patient population, the 11 living patients to whom the nurses would prefer not to provide nasogastric hydration represent only a small fraction, 18%, of the home's intellectually impaired individuals.

Notes:

1. Master AM, Lasser RP, Beckman G: Tables of average weight and height of Americans ages 65 to 94 years. JAMA 114: 125-128, 1985.
2. Dresser RS, Boisaubin EV: Ethics, law, and nutritional support. Arch Intern Med 145:122-124, 1985.
3. Meyers DW: Legal aspects of withdrawing nourishment from an incurbly ill patient. Arch Intern Med 145:125-128, 1985.
4. Seigler M, Weisbord AJ: Against the emerging stream: should fluids and nutritional support be discontinued? Arch Intern Med 145:129-131, 1985.

TABLE I

Percent of patients where treatment is considered "too aggressive" for nursing home patients based on their current status and in hypothetical circumstances of total immobility or total unresponsiveness (n=98)

	Current Status	If Immobile	If Unresponsive
Nasogastric Hydration	11	11	22
Nasogastric Feeding	31	32	46
Intravenous Fluid or Medication	42	47	66

Medical Ethics and Humanities

Treatment Decisions in a Skilled-nursing Facility:

Discordance with Nurses' Preferences

Michael L. Wolff, MD, Susan Smolen, BS, and Linda Ferrara, RN*

Hospitalization transfers from a skilled-nursing facility were studied. A hierarchically arranged questionnaire on acute medical deterioration and treatment aggressiveness was used to study the degree of discordance between the transfers actually made and the preferences of nursing home head nurses. According to the nurses, 37 per cent of the patients involved should not have been hospitalized even under the most compelling circumstances; however, 76 per cent of this subgroup had in fact been hospitalized under physician's orders. The nurses would have refrained from instituting any new treatment in 14 per cent of the cases, all of which involved chronic neurological impairments; 36 per cent of this subgroup had nevertheless been hospitalized in the 12 months prior to the study. *J Am Geriatr Soc 33:440, 1985*

The transfer of nursing home residents from nursing home to hospital is the key step in determining the extent of medical intervention. There has been very little published on the ethical issues involved, although Besdine raised the issue systematically at the 1983 annual meeting of the American Geriatrics Society and subsequently in that society's journal.[1] Case law is rather confusing to the practitioner,[2] and the extent to which legal guidance must be sought varies from state to state and is inconsistent in application.

Attempts have been made to anticipate acute illness and to designate treatment status of patients in nursing homes.[3] In addition, ethics committees have been used to make decisions in difficult cases, allowing interaction of staff members, family members, clerics, and lawyers in the consideration of subacute and chronic treatment.[4] Hilfiker has described the physician's dilemma poignantly, and the spirited letters written in response to his description outline many of the limitations of our current health care system.[5,6]

Recently, an affiliation between the Daughters of Sarah Nursing Home, a voluntary, nonprofit skilled-nursing facility, and Albany Medical College has been formed. This has allowed the collection of information from charts and from questionnaires completed by nurses and families regarding decisions to transfer patients to a hospital or to refrain from transferring patients with acute medical deterioration. This study was undertaken as a review of practices during the year prior to the affiliation of the institutions. The purpose was both to perform a systematic audit and to provide a standard against which to compare future practices in terms of documentation, family satisfaction, health outcome, and hospital utilization. It was also necessary to develop a base of information on recent practices in anticipation of both life-protective and utilization-minimizing constraints, which are certain to create increasingly grave ethical conflicts for the medical practitioner in the years ahead.

While very few decisions were made to treat life-threatening illnesses in the nursing home setting, the decisions to hospitalize patients appeared to conflict frequently with attitudes expressed by the five head nurses of the facility. This area of disagreement is the focus of this report and is of particular importance because nurses are the professionals charged with identifying any deterioration of patients and initiating the transfer process.

Methods

SUBJECTS

The Daughters of Sarah Nursing Home is a voluntary, nonprofit skilled-nursing facility that accepts patients without regard to source of payment. There are 200 beds divided into five nursing units.

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One hundred fifty residents are classified as requiring total care, and 125 residents are diagnosed as having some form of intellectual or psychiatric impairment. Information was obtained for 100 residents, selected from alternating rooms. In addition, a sample of half (N = 20) the residents who had died in the year prior to academic affiliation was included.

The average age of the population studied was 84 years, with a median of 85 years for the living and 87 years for the deceased subjects. Men constituted 12.5 per cent and women 87.5 per cent of the population. Overall, 18 per cent had chronic neurological disorders (of which 80 per cent were progressive). Sixteen per cent were incontinent of urine alone, 1 per cent were incontinent of stool alone, and 47 per cent were doubly incontinent. There was a proven noncutaneous malignancy in 6 per cent and suspected malignancy in 4 per cent.

CHART ABSTRACTION

Each chart was examined to determine instances of acute illness for which referral to hospital was either made or considered during the resident's stay in the home up to July 1983, when academic affiliation occurred. The sources for such information were (1) a flow sheet documenting transport to hospital for either emergency room care or direct admission and (2) monthly summaries of the resident's health status entered by the registered nursing staff. Cross-reference was then made to physicians' and nurses' progress notes and, where applicable, to hospital discharge summaries. Information on the organ system(s) involved in each episode of illness was recorded. Types of chronic impairment were similarly documented.

In addition, the patient's age, sex, mental status, functional status (as indicated by the most recent New York State DMS-1 score), and legal guardian or conservator were recorded. Documentation of consultation with the resident or with his or her family members on the decision to hospitalize or not hospitalize the resident was sought. In addition, documentation of discussions and conclusions pertaining to treatment status was sought, i.e., institutional locus, initiation of new treatment, designation of resuscitation status, and compliance with the wishes of residents or their families.

FAMILY QUESTIONNAIRE

A questionnaire was administered over the phone, when possible, or by mail to the next of kin. They were asked to recall the previously listed instances of acute illness and to describe who notified them, when they were notified of the decision to hospitalize, and whether they agreed with the decision in terms of locus and intensity of therapy. After several interviews, it became apparent that many details were difficult for family members to recall, so subsequent collection of information was restricted in each case to the two most recent episodes of illness. Another limitation in gathering data was our feeling that it would be countertherapeutic to question the residents themselves about treatment decisions in a broad manner at the time this study was done, prior to delineation of the current practices in the home and more thorough acquaintance of the newly affiliated physicians with individual patients.

NURSING QUESTIONNAIRE

The head nurse on each of the five units was asked to complete a questionnaire on each subject in the study. The nurses were personally familiar with the individual subjects and had been in charge of their nursing care for between 11 and 48 months. Questions were first arranged hierarchically, with the patient described as being in progressively poorer chronic medical condition and the question posed as to whether hospitalization would be appropriate given a particular acute situation, i.e., fever, unresponsiveness, seizure, hematuria, gastrointestinal bleeding, aspiration, hypotension, joint inflammation, and cardiac arrest. Then a hierarchy of procedures was described (nasogastric hydration, nasogastric feeding, administration of intravenous fluid or medication, transfusion, surgery, dialysis, bronchoscopy, endoscopy, and intubation) and the nurses were asked to decide whether the procedure would be inappropriate for each patient as functioning currently, if subsequently immobile, and if permanently unresponsive. A score of 1–10 was thus assigned (from least to most aggressive treatment) for each level of dysfunction (see Appendix). The first "yes" answer designated the score—for instance, if nasogastric hydration were deemed inappropriate, the score would be 1; if nasogastric feeding were deemed inappropriate, the score would be 2; and if there were no "yes" answer, the score would be 10.

Results

Of the 100 living subjects, 64 experienced 174 instances of illness requiring referral to hospital for diagnosis or treatment. There were 37 nonterminal illnesses among 11 of the 20 subsequently deceased individuals. There were thus 211 nonterminal illnesses among the 120 subjects for which hospitalization or emergency room treatment might reasonably have occurred. The difference in the rates

TABLE 1. Hospitalization Considered Appropriate by Head Nurses

	Current Patients (N = 98)		
Symptom	Current Condition n (%)	If Immobile n (%)	If Unresponsive n (%)
GI bleeding	62 (63)	53 (54)	13 (13)
Unresponsiveness	45 (46)	37 (38)	NA
Aspiration	36 (37)	31 (32)	8 (8)
Joint pain/swelling	36 (37)	17 (17)	4 (4)
Seizure	31 (32)	19 (19)	4 (4)
Fever	24 (24)	10 (10)	3 (3)
Hematuria	21 (21)	9 (9)	3 (3)
Arrest	19 (19)	12 (12)	3 (3)
Hypotension	16 (16)	4 (4)	3 (3)

of nonterminal illnesses for the living and the deceased subjects was trivial. Overall, the organ systems affected were as follows: musculoskeletal (25 per cent), cardiovascular (19 per cent), gastrointestinal (17 per cent), respiratory (16 per cent), and others in smaller proportion. In approximately 30 per cent of instances, discussions with family members were not recorded in the nursing home charts. All of these instances were accounted for by the fact that notification occurred after hospitalization, according to the families. Spouses were rarely consulted, and offspring were frequently consulted. The family's reaction to treatment decisions was not recorded in 78 per cent of instances. There were three instances in which family disagreement was noted in the charts, and families reported an additional four instances of disagreement (3.3 per cent). In only seven instances was a choice made to keep a subject in the nursing home, and in only four instances was a decision made not to institute new treatment. The head nurse of the home was the most frequent notifier of families.

The nursing questionnaire was remarkable for revealing a more conservative treatment orientation than was apparent in actual treatment activities. Because of change in head nurse staff, this questionnaire was answered regarding only 98 of the living and 17 of the deceased patients. Table 1 shows that of the living patients, a maximum of 62 subjects (63 per cent) were considered to require hospitalization under the circumstances described. Conversely, for 37 per cent of living patients, the head nurses considered hospitalization inappropriate under the circumstances described; this proportion increased to 46 per cent with the hypothetical circumstance of total immobility and to 87 per cent with the circumstance of unresponsiveness. At all three disability levels, gastrointestinal bleeding provided the most compelling impetus for hospitalization. Transfusion was considered too aggressive for 55 per cent of patients at their current ability levels, for 72 per cent if immobile, and for 95 per cent if unresponsive, suggesting that hemodynamic stabilization without transfusion would be the nurses' goal for hospital transfer in a fraction of instances.

The scores for treatment aggressiveness similarly declined with hypothetically decreasing functional status. On average, head nurses felt that the patients either at current functional status (intervention score = 3.97, range 1–10) or immobilized (3.39, range 1–6, $\chi^2 = 4.90$, $p < 0.03$ versus current status) should receive intravenous fluids or medication, if necessary, but not transfusions, and that they should not receive even intravenous fluids if rendered unresponsive (2.75, range 1–5, $\chi^2 = 6.54$, $p < 0.01$ versus immobilized). Only the retrospectively considered deceased patients who were hypothetically unresponsive were consistently judged as not warranting nasogastric nutrition, though the head nurses felt that even these individuals should be given nasogastric hydration. For only 31 living patients could head nurses conceive of an instance in which termination of treatment would be appropriate. However, dialysis was considered inappropriate in 97 per cent of cases at current functional status, and bronchoscopy, endoscopy, and intubation were considered appropriate in 82 per cent. All four of these procedures were considered universally inappropriate in the retrospectively considered deceased individuals. Nurses considered themselves and the physicians to be the best judges in 23 cases, and the family members—in consultation with nurse and physician—to be the best judges in 17 cases. For half the cases, the nurses stated they would advocate their position, if in disagreement with the family's, to the physician, and for an additional fifth of cases they said they would advocate their position to both the family and the physician. Only one patient had a formally designated "do not resuscitate" status. This patient also should not have been hospitalized, according to the family, although she was hospitalized on one occasion against the family's wishes.

Transfer appropriateness and treatment intensity opinions did vary from unit to unit. This appeared to reflect the prevailing functional status of patients on the individual unit. Three of the five units have consistently had patients with greater-than-normal care requirements admitted. This is reflected in average DMS-1 scores ranging from 516 ± 55 SD on the most intensively staffed unit to 320 ± 148 SD on the least intensively staffed unit. Of interest, again, is the fact that hospitalization was sometimes felt appropriate even though the specific treatments likely to occur in hospital were felt to be too aggressive.

Of 37 living patients whom the nurses would not have hospitalized under the most compelling circumstances, 28 (76 per cent) had in fact been hospitalized for acute illness occurring in the nursing home. Eleven (30 per cent) of these hospitalizations were for falls and acute musculoskeletal trauma, including two for orthopedic surgery and five for precautionary x-rays only (despite opposing opinions on the "joint pain/swelling" item). Nine of the 36 individuals whom nurses would not have hospitalized for gastrointestinal bleeding had, in fact, been hospitalized for gastrointestinal bleeding.

Of 14 patients for whom nurses would have favored no new therapy (score of 1 on the treatment intensity scale), all had chronic neurological failure and 9 (64 per cent) were incontinent. On the DMS-1 behavioral scale, ten (71 per cent) were sometimes agitated, five (36 per cent) were sometimes assaultive, eight (57 per cent) were verbally abusive, and 12 (86 per cent) were depressed.

Overall, the results for deceased patients appeared to be similar, but the retrospective data were felt to be potentially so influenced by the known prognosis (i.e., death), that they are not reported here in detail.

Discussion

The results of this survey are interesting on several counts. The relative concordance of treatment decisions with family wishes is reassuring, as is the good reporting, by family members, of appropriate notification by the staff. The fact that spouses were rarely consulted before hospitalization was principally a reflection of the fact that the overwhelming majority of the home's patients are widowed females.

The contrast between actual practice and nurses' perceptions of what would be the appropriate intensity of care is a matter of concern. It reflects a prevalent ethical disquiet on the part of the health professionals who provide most of the daily supervision of elderly nursing home residents. It is unclear whether the physicians involved felt similar conflicts, but the fact that one-third of transfer decisions had been made before consultation with families implies that physicians continue to presume in favor of more intensive treatment and that families, subsequently, concur in such a presumption. Since head nurses were queried retrospectively, it is quite possible that they would have acted as the nurse on duty acted, i.e., that they would have notified the physician and accepted the decisions made without documented disagreement. Whether staff nurses or nurse's aides would concur with the head nurses has not been studied. These data do demonstrate, however, that the considered preferences of the senior nurses of this facility were at variance with many of the actions taken.

In many instances it appears that these nurses oppose hospitalization *per se*, as evidenced by the fact that even though the intensity of care thought appropriate by the nurses is generally beyond the use of intravenous substances, the nurses would not wish to transfer roughly one-third of this patient group. The converse was true in other cases, perhaps reflecting a perceived need for bedside monitoring (*viz*, gastrointestinal bleeding), which is difficult to provide on a low-intensity unit. Since the diagnostic and laboratory technology and staffing levels required to support intravenous therapies are among the distinctions between nursing homes and hospitals, lower-technology hospital settings or higher-technology nursing home settings may be appropriate for selected patients. In addition, falls and trauma accounted for a third of hospitalizations that the nurses might otherwise have opposed. Half of these were for precautionary x-rays and might well have been prevented had a physician or physician-extender been available at the nursing home at the time of injury.

The lower preference for intervention in the presence of immobility or unresponsiveness demonstrates that the nurses of this facility do consider quality of life when forming opinions about appropriate treatment. However, the high rate of perceived depression in individuals for whom nurses wish no new treatment implies that the nurses' views are motivated by their perception of individual suffering rather than judgments as to individual worth. As Avorn has pointed out, such secondary judgments regarding "quality-adjusted" life may be hazardous and may seriously underestimate the patient's own perception of life's worth even when life entails substantial suffering.[7]

There has been no formal attempt, as yet, to validate the scales used. These results have been presented to the head nurses and staff nurses in the nursing home. They unanimously agree that the findings presented herein do reflect their feelings. They concur that nurses have in fact not expressed disagreement with decisions, despite the implication made by the results of the questionnaire that they would have done so. They also express the belief that many unnecessary hospitalizations occur, after diagnostic work-up is complete, because of a lack of knowledge on the part of emergency room personnel as to the interventions possible and the quality of personnel available in the skilled-nursing facility. In addition, the questionnaire item relating to "termination" of care was felt to be ambiguous (see Appendix).

The selection of the patients for less intensive treatment is the nub of the question. It is unfortunate that we were unable to question the patients, but approaching even family members is difficult. We are currently convening a panel to consider what approach may be appropriate in the future. A systematic survey of the patients will require careful consideration. Many of the mentally fit nonagenarians have spontaneously said that they do not wish to go to hospital, but others have found these questions to be abstract, even in the midst of a situation in which the decision must be made expeditiously.

With regard to families, more intensive education on the ramifications, in terms of help and suffering, of high-technology interventions and a systematic approach to treatment intensity issues on or shortly after admission may prove beneficial.[3] Anecdotally, adult children of intellectually impaired patients appear hesitant to request that technological intervention be limited and generally do so with fear of criticism from the medical staff. There are no systematic data available to suggest whether families or staff members might feel differently in a nursing facility drawing more heavily on an impoverished population.

We were also unable to poll the physicians on a patient-by-patient basis, but it is clear from discussion that all of the current and past physicians of this facility have felt uncomfortable, in certain instances, with the intensity of treatment toward which they felt impelled. The current setting is ill-suited to the formal study of physicians' attitudes because of the small staff and the fact that, since the academic affiliation of the home began, one of the authors (MW) either has had or currently maintains medical responsibility for nearly two-thirds of the home's patients. There has been some evidence in the literature regarding an increasing tendency of academically based physicians to omit life-prolonging treatment for terminally ill patients.[8] There is also evidence that some 6 per cent of febrile patients in community nursing homes have had antibiotics omitted, with frequently fatal outcome, apparently by intent, in severely debilitated individuals.[9] Wanzer and colleagues have taken a clearly stated position with regard to the "levels" of treatment that may be delineated for individual patients.[10] They emphasize a physician's responsibilities and relative autonomy. Their assertions are not, however, universally agreed on or carefully buttressed by philosophical argument. They do provide some solace to members of the medical profession, for whom these issues are not abstract but rather the subject of daily concerned application.

Summary

This study quantifies the discordance between treatment locus decisions actually made on behalf of patients in a skilled nursing facility and treatment locus preferences subsequently expressed by head nurses. Such discordance is of substantial magnitude, as demonstrated by use of a hierarchical questionnaire technique.

Acknowledgments

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Appendix: Nurse's Questionnaire

I. **Patient's Name** ____________________
Unit ____________________ **Date** ____________

II. **If this patient developed one of the following findings, would you think it appropriate to hospitalize him/her if necessary for diagnosis or treatment?**

FINDING	DECISION	
	No	Yes
a) Fever	___	___
b) Unresponsiveness	___	___
c) Seizure	___	___
d) Hematuria	___	___
e) GI bleeding	___	___
f) Aspiration	___	___

g) Hypotension	___	___
h) Joint pain & swelling	___	___
i) Cardiopulmonary arrest	___	___

III. If this person were to recover from an acute illness, yet be rendered completely immobile (i.e., in need of constant supervision and care), would you think it appropriate to hospitalize under the following conditions?

	No	Yes
a) Fever	___	___
b) Unresponsiveness	___	___
c) Seizure	___	___
d) Hematuria	___	___
e) GI bleeding	___	___
f) Aspiration	___	___
g) Hypotension	___	___
h) Joint pain & swelling	___	___
i) Cardiopulmonary arrest	___	___

IV. If this person were to recover from an acute illness, yet be rendered unresponsive, would you think it appropriate to hospitalize under the following conditions?

	No	Yes
a) Fever	___	___
b) Unresponsiveness	___	___
c) Seizure	___	___
d) Hematuria	___	___
e) GI bleeding	___	___
f) Aspiration	___	___
g) Hypotension	___	___
h) Joint pain & swelling	___	___
i) Cardiopulmonary arrest	___	___

V. Which of the following therapies would you consider too aggressive to impose on *this* patient, even if they are considered to be standard therapies on other patients?

	No	Yes
a) Nasogastric hydration	___	___
b) Nasogastric feeding	___	___
c) IV fluids or medication	___	___
d) Transfusion	___	___
e) Emergency operative procedure	___	___
f) Dialysis	___	___
g) Bronchoscopy	___	___
h) Endoscopy	___	___
i) Intubation	___	___

VI. Which of these therapies would you consider too aggressive if this patient became permanently immobile?

	No	Yes
a) Nasogastric hydration	___	___
b) Nasogastric feeding	___	___
c) IV fluids or medication	___	___
d) Transfusion	___	___
e) Emergency operative procedure	___	___
f) Dialysis	___	___
g) Bronchoscopy	___	___
h) Endoscopy	___	___
i) Intubation	___	___

VII. Which of these therapies would you consider too aggressive if this patient became permanently unresponsive?

	No	Yes
a) Nasogastric hydration	___	___
b) Nasogastric feeding	___	___
c) IV fluids or medication	___	___
d) Transfusion	___	___
e) Emergency operative procedure	___	___
f) Dialysis	___	___
g) Bronchoscopy	___	___
h) Endoscopy	___	___
i) Intubation	___	___

VIII. If the family of this patient wished *more* active treatment than you thought appropriate, would you:

a) Advocate your point of view to the patient?
b) Advocate your point of view to the family?
c) Advocate your point of view to the physician?
d) Advocate your position to all above?
e) Tell no one your point of view?

IX. If the family of this patient wished *less* active treatment than you thought appropriate, would you:

a) Advocate your point of view to the patient?
b) Advocate your point of view to the family?
c) Advocate your point of view to the physician?
d) Advocate your position to all above?
e) Tell no one your point of view?

X. Who do you feel is *most* qualified to make these types of decisions?

a) Patient
b) Family
c) Nurses
d) Physician
e) Other

XI. Can you think of an event that would justify the termination of care for this patient?

No___ Yes___

If Yes, please describe.

a)
b)
c)
d)
e)
f)

41f.

Treatment Dichotomies

This issue contains an article entitled "Treatment Decisions in a Skilled Nursing Facility: Discordance with Nurses' Preferences," by Wolff, Smolen, and Ferrara. The research the authors conducted on nursing home residents through their nurses is important for at least three reasons.

First, the dichotomy between nurses' preferences regarding the hospitalization of nursing home residents and what eventually befell the residents is a modern tragedy that no doubt occurs in every long-term care institution. The tragedy is compounded not only by the unnecessary expense borne by the home residents, their families, their estates, and the public, but by the conflict of duties such a dichotomy represents. Physicians treating such patients clearly consider it a duty to preserve life through the modern, technological interventions available in hospitals. Although these treatments make sense when some kind of function can be recovered, they lose their validity when outcomes are obscure. Nurses who have been responsible for the care of such residents consider it their duty to weigh the realities of continued life against the benefits of such interventions. Because the authors did not yet have relationships with the residents, they did not interview them. Perhaps they would have discovered, as Wagner did,[1] that over half the nursing home residents would have refused certain forms of care in any event.

A better system of ascertaining residents' preferences and of acting in their behalf is necessary. That brings me to the second point. In addition to requiring all residents (or their families) to give advance directives regarding their care before admission, some mechanism is needed for updating these directives, especially as persons become more and more dependent. As this inevitable process occurs, nursing facility residents become less and less able to speak for themselves. The Wolff study implies that the nurses who care for the residents are often more capable than the patients, their families, or the responsible physicians in interpreting what treatment may or may not be appropriate. This implication needs further testing. Surely, however, policies developed in the future concerning the hospitalization of nursing home patients should include the perceptions of the nurses who take care of the patients from day to day.

The third reason the Wolff study is so important is even more far-reaching. It may be that many of us will spend almost a fourth of our lives in a different kind of domicile than that in which we are now nurtured. It is important that those who live with us in this *domus* have some say in how we are treated, since, presumably, they will know better than our own children how we think about our health care. Thus traditional notions of families, of expressed and unexpressed wishes, and of health expectations of the institutionalized elderly will change. No doubt the sheer economic impossibility of caring for a huge segment of the population will force us to establish more stringent policies about the kinds of crises that would lead to an order for hospitalization.

Would it not be better, however, to effect such changes through a renewed dedication to the meaning of being a "physician" rather than a "doctor"? An expert "physician" is one who can determine our interests and values, intervene when appropriate on the basis of this determination, and turn from intervention to comfort when the prolongation of life suits neither us nor society. A "doctor" could be one who orders tests and therapies on the basis of organ system malfunction, with little or no regard to the values and desires of patients or to their eventual functioning as persons in their environment. For now, the Wolff study suggests that the nurses in skilled nursing home facilities could help the physician to fulfill some of his traditional supporting roles in caring for the elderly.

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TASK 4. UTILIZATION IN THE HOME

Solid national statistics regarding the utilization, cost and outcome of home parenteral and enteral nutrition (HPEN) are in the developmental stages. Much in this area will depend on the success of OASIS, the Oley/A.S.P.E.N. Information System scheduled to get off the ground in 1986. A goal of this system is to develop for the first time a national patient-specific registry that will track the home patient over time so that variables such as underlying diagnosis or duration and outcome can be aggregated for a specific age group such as the elderly. In the meantime, the Oley Foundation has looked at utilization samples from several existing data sources as shown in Table I.[1] Since the absolute number of patients on home parenteral and enteral nutrition is unknown (estimates vary from 2,000-5,000 on parenteral support and 15,000-20,000 on enteral support),[2] it is important to realize that the patients in the sample groups used here are not distinct patients or groups of patients, for a particular patient may be included in at least two of the data sources, the "registries" (including the Oley/*LifelineLetter* sample) and the commercial services (see Figure I). At this point in time this is the only data available.

Demographics

Home Parenteral Nutrition (HPN) -- In terms of age distribution these samples show a similar picture. Roughly 10-20% of the patients are below 20, about half are 50 years or older, and 20% are over 65 (see Table II). Applying this percentage to the national estimates means that there are approximately 400 to 1,000 people 65 and over on parenteral support at home. This percentage in the oldest age category demonstrates a significant shift from earlier home utilization. In 1978 the New York Academy National Home TPN Registry reported that of 358 patients 30% were over 50 and only 5% were over 65. This suggests that the use of HPN has extended as experience has grown and also as the long-term survivors have reached an older age.

As shown in Table III in 4 out of the 5 HPN patient series there are more women than men, especially in the later age groups. This could reflect the greater life expectancy of women generally or that the diseases which lead to HPN are more common in women, for example, radiation enteritis following cancer of the cervix or ovary, or the professional and family perception that older women can be more readily rehabilitated than men to a functioning level that justifies the complex HPN undertaking.

Home Enteral Nutrition (HEN)--HEN data show more frequent use of this kind of therapy in older patients (see Table II). If 55% of enteral patients are over 65 and there are indeed 15,000 to 20,000 HEN patients nationally as has been "guesstimated," then 8,000 to 11,000 elderly (65+) people are receiving tube enteral feedings. It is likely that the majority of these patients are at home but a small proportion may be in health related facilities. Unfortunately there is no previous database with which to compare these figures, however one can assume that they would show a growth as the elderly population has increased and as advances have been made in HEN technology and its application.

Unlike HPN there seems to be an equal sex distribution of patients on HEN (Table III). The only exception to this generalization occurred in one small commercial series (CHNS III) where males predominate.

Cost

There are currently no figures readily available. It is thought that HPN costs, on the average, 30%-50% of the cost of providing such therapy in the hospital and HEN costs about 10%-15%. While some facts regarding charges (as distinct from cost) do exist, these are difficult to analyze because they vary considerably and various service components (e.g., delivery of supplies, nursing visits, inventory and reimbursement management) may be included in the charges for solutions and supplies. On an annual basis, charges for an adult on HPN range from $50,000 to $100,000 and for HEN from $3,000 to $12,000.

Table IV summarizes the payment mechanism of patients reported from 5 different sources. The majority of patients had more than one type of coverage, but only the principle payer is given. The high proportion of Medicare funding in the Oley group may be due to the fact that this sample includes those longer-term patients who have exhausted their private insurance and become Medicare eligible.

In regard to the older patient, the Oley Foundation looked at those responding to a consumer (patient) survey done in June, 1985.[3] Of those 60-64 (n=16), 16% reported basic Medicare coverage only, 26% reported Medicare plus supplemental, and 58% reported coverage by private carrier. Among those 65 and over responding to this survey (n=26), 4% reported Medicare coverage alone, 88% Medicare plus supplemental, and 8% Medicare plus supplemental and Medicaid.

Indications for HPEN

In initiating long-term nutrition support the issues as discussed under Task 1 "The Patient Perspective" are very important.

The criteria commonly used for selection of HPN patients are listed below:

1. Potential for meaningful rehabilitation.
2. Patient's desire and ability to accept responsibility for aseptic infusion techniques.
3. Ability of family or friends willing to support patient.
4. Availability of medical backup both for acute problems and long-term supervision.
5. Financial resources so the patient can afford HPN without great distress or anxiety.

Obviously in older patients the question of what is "meaningful rehabilition" may be harder to resolve, especially if there is likely to be great dependence on the family for managing the technical aspects. It must be stressed that few patients can afford full-time nursing support at home and nursing homes or other health related facilites rarely accept patients on HPN. Thus, relative self-sufficiency or a strong family commitment are essential. "Meaningful rehabilitation" usually implies freedom from severe pain and the likelihood of returning to normal age-related activities.

In the Albany program a great effort is made to evaluate patients and their home situation before HPN is openly discussed and then to have a patient and family conference where the pros and cons are forthrightly presented. If the decision is made to "go ahead," we have found it very valuable to arrange a visit from one or more experienced home patients, if possible close in age, sex, diagnosis, and home area to the starting patient.

In our experience, the majority of older patients are settled into their routine in two or three weeks, especially if the move from hospital to home is smoothly planned. This involves coordinating the delivery of the supplies 24 hours in advance, having them conveniently arranged in the patient's bedroom, installing an extra refrigerator if necessary, and making sure that a nurse who is familiar to the patient in the hospital is at their home when they first arrive back. All of these services are usually provided by the commercial pharmacy service.

Most HPN patients, both young and old, accept the technological dependence well and are full of pride for their medical sophistication and independence. However, about 25% of patients, most commonly those who are older, become depressed and anxious; while they may recognize their good physical rehabilitation, the real quality of this high tech existence is clearly in doubt. In such situations, a great deal of supportive "listening," small nighttime doses of an antidepressent (50-70 mg Imipramine or 100 mg Desyrel), and frequent visits from the home nurse, can cause dramatic improvement. If the anxiety depression persists, then it is often wise to firmly present the option of discontinuing HPN, even though that usually means death. This allows patients to reaffirm their sense of control and accept more actively a decision to live.

In many clinical situations, particularly with older patients, the "meaningful rehabilitation" may finally dwindle to "existing" but not "living"; especially if the underlying disease is progressing. At these junctures, the decision is gradually made to back off from complete nutrition to more limited fluid support. This decision process involves the patient, doctor, and the close family; and is quite easily recognized and moved through. In Albany and many other large programs, patients with cancer and bowel obstruction may be considered for HPN if they are comfortable and can be expected to live several months. In such situations, the hospital training period is shorter and the technical burden simplified by using a modified nutrient solution from the onset. Such solutions do not meet the patient's calorie and protein needs but they keep the patient hydrated and comfortable. It is an option which many patients and families choose, even though they know gradual weakness and weight loss are inevitable as their cancer progresses. (See below, "Duration and Mortality" for HPN outcome in relation to diagnosis.)

Financial worry, especially as it relates to this very expensive therapy, is a major concern for most HPN patients and their families. Fortunately, at this time, it is possible to reassure Medicare patients that most of their costs will be covered and that their home service will assist them with their billing problems. Relieving patients of these worries is a major contribution to their welfare.

While the decision to use HEN may be very similar to HPN and the rehabilitation potential the same or brighter because the gastrointestinal tract is only partially compromised, there are other circumstances in which the HEN is more akin to provision of baseline support as, for example, in a patient with irreversible brain damage. The majority of such cerebrally impaired patients would probably be discharged to a health related facility rather than home because they require around-the-clock nursing and the neurological deficit contributes to psychosocial detachment. The ethical decision to maintain good nutrition in patients with severe neurological impairment is best determined by a societal viewpoint, not a medical judgement.

In the situation where gastrointestinal dysfunction is borderline, for example the adolescent with infammatory bowel disease who maintains his weight but has impaired linear growth, HEN may be the necessary boost to restore growth. In these circumstances the HEN is usually taken overnight by self intubation. This type of indication is rare in older patients, but can occur in chronic disorders such as cirrhosis, renal failure, or chronic pulmonary disease where nutritional support by overnight feedings restores a level of well being that allows the patient to resist intercurrent infections and maintain reasonable health and function. Since older patients are less adept at learning self intubation, a small bore gastrostomy or jejunal tube may be more acceptable. Although it is always a possibility that in borderline situations HPEN could be overused by clinical enthusiasts, a natural and substantial break on such abuse is the strong patient preference to live free of tubes and complex technology. Only when patients and their families experience a quantam leap of better health and well being will they persist with such complex endeavors. On occasion an HPN patient may "graduate" to HEN once severe malnutrition has been corrected and an impaired gut is beginning to work a little better. However, once a patient has learned HPN they find intravenous infusion rather simple and the prospect of switching to self intubation or a permanant gastrostomy or jejunostomy is not attractive, especially if they have an ostomy and greater use of the gut can provoke greater ostomy output and the complication most feared, that of the ostomy bag overfilling and leaking. Thus in general, patients accept HEN better if they use the gut from the outset, even if more constant infusion is necessary while the patient and their bowel improve. As rehabilitation occurs, faster and more restricted infusion hours are usually possible.

Medical Diagnosis Leading to HPEN

Table V summarizes the main diagnostic groups of patients discharged on HPN. From all series except one, the most common diagnosis was malignancy. This exception was patients responding to the Oley/LifelineLetter questionnaire. This again reinforces the idea that patients who request this newsletter are disproportionately long-term survivors on HPN, probably without active cancer.

Table VI summarizes the very limited diagnostic data on HEN patients. Swallowing disorders due to a malignancy or a neurological deficit due to stroke predominate except in the Oley sample were once again more begnin, less terminal diagnoses occur.

In regard to specific diagnoses for the elderly, data is even scanter. Data available from three sources is presented in Table VII. Two sources (the commercial registry and the Oley consumer sample) show radiation enteritis and Crohn's as major diagnoses with the commercial registry also showing several patients 65+ with malignancy. In the AMC 65+ group, diagnoses are fairly evenly dispersed while in the younger group malignancy predominates as this group includes several patients who were receiving basically just fluid and electrolytes.

Duration and Mortality

Specific information regarding duration of therapy in the elderly has not been documented. Data from the New York Academy Registry shows that just over half of all the patients starting HPN are still on therapy at the end of one year, that a quarter are dead and the rest are alive but off HPN. Many of the larger, more established HPN programs have patients who have survived over 10 years on therapy at home. Average survival time obviously depends greatly on the underlying diagnosis and the population surveyed. Thus, in the Oley/*LifelineLetter* sample respondents have lived on HPN or HEN for an average of 3 years. Looking at the older patients who answered the consumer survey, those between the ages of 60-64 (n=15) had survived an average of 4.4 years (including one enterally supported patient on therapy for 61 months) and those 65+ (n=25) had survived an average of 3.18 years (including one enteral patient who had been on therapy for 17 months). These samples, however, do not include any deceased patients so obviously do not give the true picture regarding duration and mortality.

The commercial registry shows the average duration of enteral therapy to be 1.1 years and parenteral therapy to be 2.5 years with no specific figures for the elderly. One industry source (CHNS II) described 33% of their HPN patients as on therapy for three months, 8% as on for 4-12 months, and 59% as on for more than a year, again without age breakdowns.

Looking more closely at diagnosis in terms of duration and mortality, an analysis had been done of the AMC program's adult patient experience with HPN. Since 1973, this program has discharged and followed 82 HPEN patients. Sixteen of these patients had cancer and bowel dysfunction, their average age was 58.9 years, ranging from 30-78 with seven 60 or older.

Thirty-six of the patients had extreme short bowel syndrome due to Crohn's, mesenteric infarct or radiation enteritis. None of this last category had any evidence of recurrent cancer; their average age was 55.6 years, ranging from 21-84 with fourteen 60 or older. (For this analysis all patients under 20 years and those with normal bowel length such as pseudo obstruction or severe hyperemesis gravidarum were excluded.)

As shown in Figure 2, 50% of the cancer patients survived only six months and 15% survived a year. All deaths were due to the underlying malignancy. In contrast, over 50% of the patients with no malignancy have survived 3 years and 15% are still alive at 8 years. While all the malignancy patients have died, only 10 of these 35 non-malignant patients have died.

There is no available data for "cancer" versus "non cancer" outcome for HEN patients. The Albany experience with HEN adults is too small (8 patients) for a meaningful comparison.

Morbidity and Rehabilitation

The frequency of hospital readmissions is one way to gauge the morbidity of patients on home nutritional support. However, this information has not been specifically compiled for the elderly nor for patients on HEN. In 1983 the New York Academy found that three quarters of all HPN patients had no HPN related readmissions during that year. Fifteen percent had one readmission and 11% had two readmissions or more. The commercial registry data for 1984 shows a similar picture. Steiger and Srp[4] found that over five years (1976-81) their HPN patients with Crohn's, radiation enteritis, and mesenteric infarct spent on the average about 13% of their time in the hospital. About a quarter of this hospital time was related to HPN complications. One in five of their patients was not rehospitalized at all during the 5-year study period. This low rehospitalization rate attests to the efficacy of HPN, since home management is obviously cost saving compared to institutional care.

As shown in Table VIII sepsis or suspected sepsis is clearly the most common reason for readmission. In 80% of the patients with suspected sepsis, infection was confirmed by blood culture. A bacterial infection was six times more frequent than a fungal infection. In that same year (1983) 1 out of 8 patients with suspected sepsis was managed as an outpatient.

Potential complications for both enteral and parenteral feedings were outlined in Task 1, Tables I and VII, respectively. Very long-term nutrition support with a defined formula diet does have some rather far-reaching implications in terms of completeness of the artificial diet. Even in healthy individuals nutrient requirements are only firmly established for some trace elements and even some vitamins are only approximately agreed upon. From a reasonable variety of foods and by metabolic regulation of absorption and excretion, it would seem that healthy subjects meet their requirements. However disease and diet restriction alter this set of assumptions and for patients dependent upon long-term enteral or parenteral therapy more data is needed about their nutrient requirements and the influencing variables. Table IX lists some of the potential factors that may operate in these circumstances. In fact HPN has lead to a number of obscure deficiency syndromes, which in some instances have helped to clarify the metabolic role of several micronutrients. These syndromes are listed in Table X, along with references to the articles where they are discussed.

Table XI gives the rehabilitation status of HPEN patients as reported in 5 sources. Unfortunately the method of describing rehabilitation is not uniform from one series to another, which may explain some of the discrepancies. However, generally it would seem that 50-60% of HPEN patients are able to work part time or full time, 15-20% are retired or of preschool age and 20-30% are unable to work. Forty-two percent of those responding to the Oley survey described themselves as carrying on normal activity for their age. Of those 60-64 (n=19) from this sample, 37% reported that they were able to carry on normal activity for their age and 44% of those 65 and over (n=27) reported the same.

The majority of specific comments from these older respondents indicated satisfaction with their quality of life and a very positive rehabilitation. The most frequent comment was appreciation for the ability to be at home and the energy nutritional support gave them for activities such as entertaining, camping, volunteer work and other community activities. One older respondent (age 64) continued to work full-time outside of the home.

Forty-four percent of those 60 and over also thought that respite care was or would be important if they or their family caregiver became incapable. One spouse felt that her own health was going "down hill" because of a lack of respite. This percentage among the elderly is higher than the sample as whole which registered 32% as seeing a need for such relief.

Procedures, Equipment, and Formulas

Currently there are no special adaptations of the technology tailored to the needs of the elderly HPEN patient; they or their caregivers, as with all patients, must learn the technology. In terms of HPN patient training, New York Academy Registry data from 1981 show the mean training time required before discharge is longer for patients learning home mixing (30.4 ± 17.8 hours) than for those being provided with pre-mixed solutions (21.6 ± 16.9 hours). Also hospital readmissions tended to last 7 days longer for the home-mixing patient.

Under the DRG reimbursement system 5 days are allowed for HPN patient training. The Albany experience indicates that 10 days to 2 weeks is a more realistic time span. Patients are usually ill prior to their catheter insertion and their underlying illness coupled with soreness from the insertion procedure make it difficult for them to concentrate immediately.

Stiffness in the joints and decreasing vision make it more difficult to measure additives with syringes so the older patient may need to have pre-mixed solutions. They also frequently require a family member or some other person to help connect tubing and administration sets to complete an HPN "hookup." As mentioned in Task 1, going to the bathroom while infusing may be particularly difficult for the older person and nessitate the availability of a bedside commode

From the HPEN patient point of view the availability of premix formulas and the development of a pump with better mobility are extremely important. In the Oley consumer survey patients rated use of premix solutions as the most important home service option (see Table XII).[3] This held true for those 60 and over who gave it a 1.03 on a scale of 1 (important) to 3 (least important). One could assume that with the infirmities of age any features that make home nutritional support less complex and more manageable are particularly desirable. Indeed, as one 66-year-old homemaker wrote, "I like the pre-mixed as home mixing is very time consuming and hard to do when your fingers are stiff."

Since most people judge according to their own experience, the experience of respondents was also asked in the consumer survey. Table XIII shows that experience greatly influenced the patient's preference. For this reason perhaps the most objective ranking was from the patients who had experienced more than one type of service. Patients who had home mixed their own solution and received pharmacy premixed solution, clearly preferred the convenience of premix. On the issue of nursing visit, most patients thought the first visit was important particularly if they had met the same nurse in the hospital prior to discharge. Home delivery of supplies was widely appreciated especially when it involved the home care service itself rather than a common carrier. However, there were several comments about the lack of consumer control of the time of delivery and delivery of wrong items.

Inventory keeping was a controversial issue among the respondents as a whole. Most thought it may be necessary and helpful to have the supplier do the inventory at first, but after a while patients felt they kept their own inventory better. Those 60 and over generally agreed with this and rated inventory by the service as just "somewhat important" (2.0), some remarking that "we work together on it" and "only I know how much I use."

Reimbursement seemed to be a constant headache for most patients, particularly when multiple carriers were involved. Those 60 and over agreed with this and rated reimbursement management as an "important" 1.18.

Provision of Service and Quality of Care

In the early years, services provided to HPEN patients were bareboned. The patients picked up their infusion supplies from the hospital pharmacy in boxes and crates and transported these supplies home in their cars and carried them in and stacked them. If the parenteral solutions were supplied premixed this usually required a weekly trip to the hospital and a second refrigerator at home for solution storage. In general, patients or their families were taught the infusion technique by the hospital staff and post discharge visits from the VNA or other domicillary nursing services were discouraged, since these professionals had not been trained to administer parenteral infusions and did not have much experience with tube feedings their involvement tended to provide more confusion than benefit.

As HPEN became more established commercial services offering special support mushroomed. Pharmacists and the pharmaceutical industry recognized this arena as one for potential expansion and a great many specialized nutrition service companies developed. Some were divisions of large national pharmaceutical solution companies, others were free standing, both national and local. The services patients receive are considerably more extensive than those provided by the early no-frills-attached programs. Delivery of supplies and stacking them on shelves is usually included, as are follow-up visits by specially trained nurses, help with inventory keeping, and supply ordering. The companies in large measure take over all the third party billing problems for their home patients and protect them as much as possible from financial harrassment. On occasions this has meant the company absorbing losses where coverage was inadequate or non existent. While reimbursement for HPN has been largely met, reimbursement for HEN services has been far less assured and many companies have withstood heavy losses in this area.

In some instances the nursing support services can be billed and are paid directly by third parties, but in many instances such services are not reimbursable and so the cost of this service component has to be buried in the solution charge. This explains in part the marked cost increase in HPEN when patients switched from hospital-based programs to commercial programs. Further, the commercial services also extended the use of HPEN by offering physicians the services of nurses and pharmacists to train and monitor their home patients, spreading the availability of this therapeutic option to many physicians who were not experienced with nutritional support.

Recognizing the proliferation of home support beyond major hospital-based programs, the American Society for Parenteral and Enteral Nutrition in 1984 adopted minimal acceptable standards of care for the home patient and they are included in Appendix A. These standards spell out the areas of responsibility, stressing that there be a clearly defined physician initiating and coordinating home nutritional support, and emphasize the need for the documentation and monitoring of the therapeutic plan.

While these standards provide the foundation, their implementation on a national scale needs to be monitored. This would not only help ensure the safe delivery of home nutritional support but also help establish a national referral network for primary care physicians needing linkage to physicians with expertise in management of the home patient.

Notes

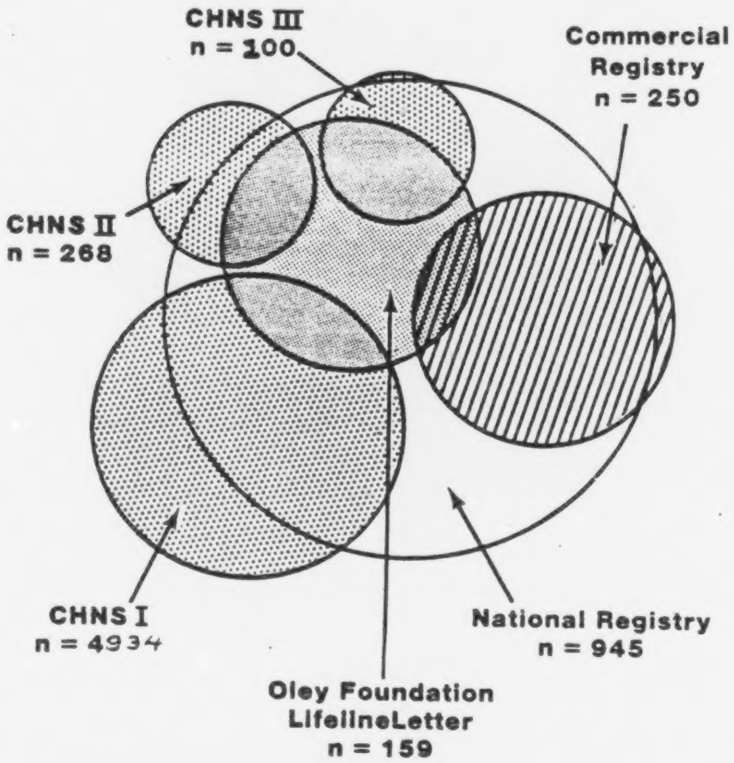
1. Howard L, Heaphey LL, Timchalk M: A review of the current national status of home parenteral and enteral nutrition (HPEN) from the provider and consumer perspective, Oley Foundation, August 1985 (submitted for publication). Tables, figures and other information from this review have been adapted by the authors for inclusion in this report.

2. Various sources such as Homecare, May 1984; Parenteral and Enteral Nutrtion, USA, 1984, C. H. Kline and Co.

3. A consumer questionnaire was mailed to 418 LifelineLetter patient subscribers in June, 1985. In the subsequent 6 weeks, 172 patients returned the questionnaire.

4. Steiger E, Srp F: Morbidity and mortality related to home parenteral nutrition in patients with gut failure. Am J Surg 145:102-5, 1983.

Fig. 1.
THE OVERLAPPING DATA SOURCES.*



*Drawn to conceptualize how a particular patient may appear in one or more data source. Not drawn to scale.

CHNS-Commercial Home Nutrition Service

Figure 2.

Survival Time in Months of Albany Medical Center Patients on HPN With Malignant and Non-Malignant Disease.

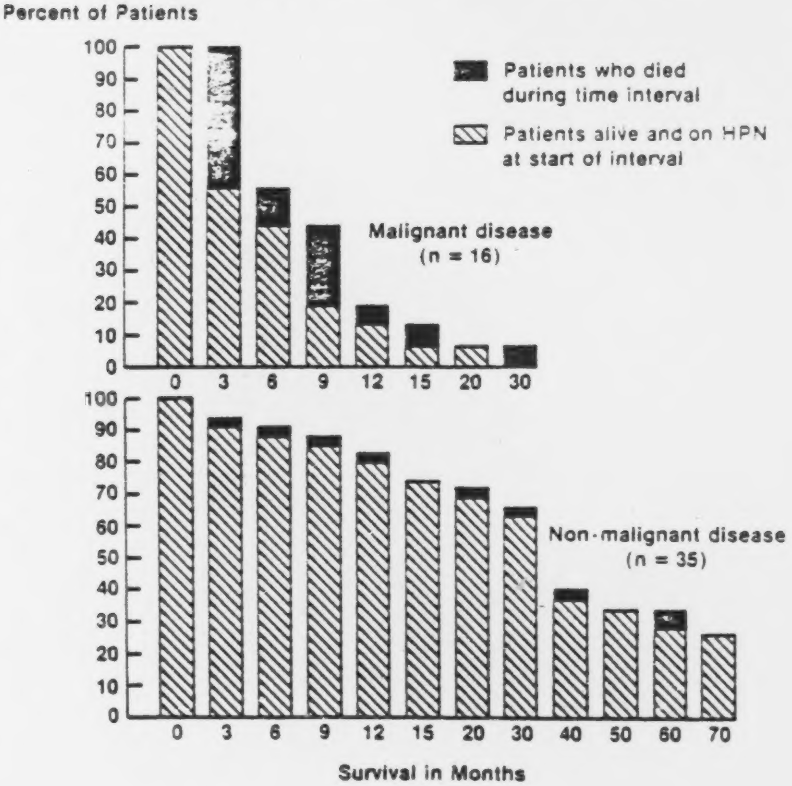


TABLE I

Source and characteristics of the utilization data

Source	Sample and Time Frame	Comment
National Registry New York Academy	945 patients-all HPN. Data from 93 programs, collected Jan-Dec 1983.	Data supplied by MD or designee supervising program in aggregate numbers.
Oley Foundation/ LifelineLetter Respondents	159 patients-153 HPN, 6 HEN. Data collected Feb-Apr 1985.	Data supplied by patients responding to a questionnaire.
Commercial Registry	250 patients-224 HPN, 26 HEN. Data collected Jan 1984-Apr 1985.	Data supplied by MD or designee supervising program receiving supplies from one national pharmaceutical service.
Commercial Home Nutrition Service I	4934 patients-2244 HPN, 2690 HEN. Data collected Jan 1984-Apr 1985.	Data supplied by home nutrition service company.
Commercial Home Nutrition Service II	268 patients-all HPN. Data collected Mar & Apr 1985.	Data supplied by home nutrition service company.
Commercial Home Nutrition Service III	200 patients-89 HPN, 111 HEN. Data collected Jan-Dec 1984.	Data supplied by home nutrition service company.

TABLE II

Age distribution of patients utilizing HPEN expressed in decades and as percentage of total number of patients reported

Age	National Registry (n=465)	Oley Foundation (n=153)	Commercial Registry (n=224)	CHNS* I (n=2244)	CHNS II (n=268)	CHNS III (n=89)
a)Parenteral						
0-10	9	12	16	6	18	16
11-20	6	2	7	4	7	18
21-30	13	6	11	9	17	9
31-40	14	19	10	13		3
41-50	14	17	11	14	32	2
51-64	27	24	25	28		24
65+	17	15	20	29	26	27
b) Enteral		(n=6)	(n=26)	(n=2690)		(n=111)
0-10		17	4	9		16
11-20		0	4	3		6
21-30		0	0	3		0
31-40		17	12	3		4
41-50		33	12	5		6
51-64		17	15	19		16
65+		17	54	59		52

*CHNS=Commercial Home Nutrition Service

TABLE III

Sex distribution of patients utilizing HPEN expressed as percent in each decade from five sources on Table I

Age	National Registry (n=465)		Oley Foundation (n=148)		Commercial Registry (n=248)		CHNS I (n=2244)		CHNS III (n=89)	
a)Parenteral	M	F	M	F	M	F	M	F	M	F
0-10	NA*		50	50	NA*		52	48	50	50
11-20			0	100			58	42	44	56
21-30			67	33			43	57	37	63
31-40			33	67			43	57	33	67
41-50			40	60			43	57	50	50
51-60			57	43			42	58	64	36
61-64			45	55			43	57	43	57
65+			35	65			38	62	58	42
Total	43	57	44	56	46	54	42	58	51	49
b)Enteral			**		(n=26)		(n=2690)		(n=111)	
0-10					NA*		56	44	59	41
11-20							58	42	100	0
21-30							49	51	0	0
31-40							41	59	50	50
41-50							58	42	71	29
51-60							55	45	78	22
61-64							60	40	67	33
65+							48	52	61	39
Total					50	50	51	49	65	35

*NA = Not available, sex by decades and therapy could not be aggregated.
**Sample of 6 was too small to include.

TABLE IV

Major funding mechanism for HPEN patients, expressed as percent of the total number of patients in each group

Funding source	National Registry[a]	Oley Foundation	Commercial Registry	CHNS II	Albany Medical Center Program[b]
Medicare	36	47	32	30	37
Medicaid	14[c]	5	8	6	17
Private ins. or other coverage[d]	47	39	58	64	41
None	3	4	2		1
No response		5			

[a] Data collected in 1980 from 63 programs and 374 patients
[b] Albany Medical Center HPN program-82 patients; 1973-85
[c] Medicaid and other welfare medical insurance
[d] "other"coverage includes VA funding, trade union funds, Crippled Childrens Services, etc.

TABLE V

Percentage of HPN patients in different diagnostic categories from all of the reporting sources listed in Table I and the AMC Program

Diagnosis	National Registry (n=465)	Oley Foundation (n=153)	Commercial Registry (n=224)	CHNS I* (n=2244)	CHNS II (n=268)	CHNS III (n=89)	AMC** (n=82)
Malignancy	42	10	25	28	41	48	32
Crohn's disease	19	40	20	26	12	9	22
Ischemic bowel (mesenteric infarct)	9	9	7	ND***	ND	1	16
Motility disorder	5	7	14	2	3	4	4
Congenital bowel disorders	4	4	9	ND	ND	2	9
Other (includes SBS unrelated to above, immune disorders and hyperemesis gravidarum)	17	30	25	44	44	34	18

*CHNS=Commercial Home Nutrition Service
**AMC=Albany Medical Center HPN Program, includes patients from 1973 to August, 1985
***ND=None diagnosed as such

TABLE VI

Percentage of HEN patients in different diagnostic categories
from three reporting sources

Diagnosis	Oley Foundation* (n=6)	CHNS I** (n=2690)	CHNS II (n=111)
Malignancy	0	40	46
Neurological disorders of swallowing	17	46	21
Other (including metabolic disorders leading to non-malignant fistulas, growth failure in inflammatory bowel disease, etc.)	83	14	33

*Oley Foundation Consumer Survey, June 1985. Among 172 respondents, 13 were on enteral support.

**CHNS=Commercial Home Nutrition Service

TABLE VII

Percentage of HPEN patients 61 and over in different diagnostic categories from three data sources

Diagnosis	Albany Medical Center*	Oley Foundation**	Commercial Registry
a)Age 61-64	(n=13)	(n=16)	(n=18)
Radiation Enteritis	15	18	16
Crohn's Disease	8	25	22
Mesenteric Vascular Disease	15	19	6
Malignancy	54	0	6
Other***	8	38	50
b)Age 65+	(n=14)	(n=25)	(n=63)
Radiation Enteritis	21	24	16
Crohn's Disease	21	24	8
Mesenteric Vascular Disease	29	16	6
Malignancy	21	4	13
Other***	7	32	57

*Albany Medical Center (AMC) Clinical Nutrition HPEN program, 1973-1985.
**Patients responding to Oley Foundation Consumer Survey, June 1985.
***Other includes, for example, scleroderma, pseudo-obstruction, trauma, motility disorder, etc.

TABLE VIII

Reasons for HPN related hospital readmissions* National Registry 1983

	Admissions	
	Total	Per 100 patient months
Sepsis, suspected or confirmed	237	3.1
Catheter related problems	62	0.8
Change of catheter	31	0.4
Fluid/electrolyte problems	24	0.3
Organ failure/dysfunction	11	0.1
Metabolic bone disease	8	0.1
Retraining in HPN technique	7	0.1
Patient/family unable to cope	5	0.0
Iron therapy	4	0.05
Other causes	14	0.2

*416 readmissions for an average length of stay of 12.9 days. Average of 0.4 readmissions per patient per year.

TABLE IX

Factors that may influence nutrient requirements for patients with gastrointestinal disorders receiving enteral or parenteral feeding

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1. Adherence of nutrients to the containers, tubes or filters used for their delivery.
2. Impaired digestion and absorption of nutrient.
3. Loss of abnormal amounts of endogenous nutrients because of interrupted enterohepatic cycles (B12, folate ?, fat soluble vitamins, zinc, copper, magnesium, calcium) that normally lead to nutrient conservation.
4. Abnormal metabolism because of systemic infusion rather than portal delivery in parenteral nutrition, leading to immediate renal excretion rather than hepatic storage of nutrients and their conversion to a functional form.
5. Altered nutrient utilization because of nighttime infusion with changed diurnal rhythms.

TABLE X

Nutrient deficiencies described in patients on long-term parenteral feeding

Nutrient	References*
Essential fatty acids	1,2
Calcium	3,4
Phosphorus	5,6
Zinc	7
Copper	8
Manganese	9
Chromium	10
Molybdenum	11
Selenium	12
Biotin	13
Folic Acid	14
Vitamin A	15
Vitamin D	16,17
Vitamin E	18

*Refer to numbers on following 2 pages for articles describing the specific nutrient deficiencies.

Table X (cont.)

1. Riella MC, Broviac JW, Wells M, et al: Essential fatty acid deficiency in human adults during total parenteral nutrition. Ann Int Med 83:786-789, 1975.

2. Wene JD, Connor WE, DenBeste L: The development of essential fatty acid deficiency in healthy men fed fat-free diets intravenously and orally. J Clin Invest 56:127-134, 1975.

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4. Shike M, Harrison JE, Sturtridge WC, et al: Metabolic bone disease in patients receiving long-term total parenteral nutrition. Ann Int Med 92:343-50, 1980.

5. Gaddock PR, Yawata Y, Van Santen L, et al : Acquired phagocytic dysfunction: A complication of the hypophosphatemia of parenteral hyperalimentation. NEJM 290:1403-1407, 1974.

6. Travis SF, Sugerman HJ, Ruberg RL: Alterations in red cell glycolytic intermediates and oxygen transport as a consequence of hypophosphatemia in patients receiving intravenous hyperalimentation. NEJM 285:763-768, 1971

7. Okada A, Takagi Y, Irakura, T, et al: Shin lesions during intravenous hyperalimentation zinc deficiency. Surgery, 80:629-635, 1976.

8. Heller RM, Kirchner SA, O'Neil JA, et al: Skeletal changes of copper deficiency in infants receiving prolonged parenteral nutrition. J Pediatr 92:947-949, 1978.

9. Doisy EA: "Effects of deficiency in manganese upon plasma levels of clotting proteins and cholesterol in man". In: Trace Element Metabolism in Animals. Hoekstra, WG, et al eds. 2:668-70, Baltimore:Baltimore Univ. Press, 1974.

10. Jeejeebhoy KN, Chu RC, Marliss EB, et al 4: A Bruce Robertson chromium deficiency, glucose intolerance and neuropathy reversed by chromium supplementation in a patient receiving long-term parenteral nutrition. Am J Clin Nutr 30:531-538,1977.

11. Abumrad NN, Schreider AJ, Steele D, et al: Amino acid intolerance during prolonged total parenteral nutrition reversed by molybdenum. Clin Res 27:621A,1981.

Table X (cont.)

12. VanRij AM, Thompson CD, McKenzie JM, et al: Selenium deficiency in total parenteral nutrition. Am J Clin Nutr 32:2076-2085,1979.

13. Mock DM, deLorimer AE, Liebman WM, et al: Biotin deficiency an unusual complication of parenteral alimentation. NEJM 304:820-822,1981.

14. Wardrop CAJ, Lewis MH, Tennant GB, et al: Acute folate deficiency associated with intravenous nutrition with amino acid sorbitol ethanol: Prophylaxis with intravenous folic acid. Br J Hematol 37:521-526,1977.

15. Howard L, Chu R, Feman S, et al: Vitamin A deficiency from long-term parenteral nutrition. Ann Int Med93:576-577,1980.

16. Klein GL, Horst RL, Norman AW, et al: Reduced serum levels of 1,25 dihydroxyvitamin D during long-term total parenteral nutrition. Ann Int Med 94:638-643, 1981.

17. Shike M, Hanson J, Sturtridge W, et al: Metabolic bone disease in patients receiving long term total parenteral nutrition. Ann Int Med 92:343-350, 1980.

18. Howard LB, Chu R., Ovesen L: Vitamin E requirements for patients on home parenteral nutrition. JPEN 3:315, 1979. (Abstract)

TABLE XI

Rehabilitation status of HPEN patients expressed as % of patients responding

	National Registry (n=615)	Oley Foundation (n=165)[a]	Commercial Registry (n=152)	Albany Medical Center HPN Program (n=82)	Univ. Washington HPN Program[b] (n=42)
Full-time employed, in school or college, homemaker	32	52	32	32	21.4
Part-time worker, student	12	7	7	23	ND[c]
Unable to work or go to school	24	11	30	18	26.2
Retired	13	19	14	15	16.7
Preschool child	6	9	ND	10	ND
Able to work but unemployed due to inability to find a job or insurance restriction on working	10	ND	5	4	35.7[d]

[a] Total number of 172 respondents answering the rehabilitation section of a consumer (patient) survey conducted in June, 1985.

[b] Robb R, Brakebill J, Ivey M, et al: Subjective assessment of patient outcomes on home parenteral nutrition. Am J Hosp Pharm 40:1646-50, 1983.

[d] 80% because they feared loss of coverage
20% because of time in HPN involvement

TABLE XII

Consumer (patient) overall ranking on
Home Nutrition Service (HNS) options[a]

Option	Score[b]
1. Premix rather than home mix	1.15
2. Home delivery rather than self pick up	1.18
3. Reimbursement management by HNS	1.19
4. Initial nurse visit	1.47
5. HNS delivery rather than common carrier	1.55
6. Home mix rather than premix	1.71
7. Respite care	1.92
8. Inventory management	2.04
9. Follow-up nursing visits	2.04

[a] This overall ranking does not take into account the patients' experience

[b] Score: 1=important 2=somewhat important 3=not important

TABLE XIII

Tabulation of consumer (patient) ranking of home services
Score: 1=important 2=somewhat important 3=not important

SERVICE	CONSUMER EXPERIENCE	PREFERENCE	
Solutions		Premixed by pharmacy	Home mixed by patient
	Premixed (n=87)	1.01	2.37
	Home mix (n=37)	1.73	1.18
	Both (n=45)	1.01	2.37
Home visits from nurse		Initial visit	Periodic follow-up visits
	None (n=44)	1.89	2.27
	Some (n=127)	1.38	1.98
Delivery mechanism		HNS* delivery vs patient pick up	HNS delivery vs common carrier delivery
	HNS delivery (n=59)	1.10	1.08
	Common carrier (n=22)	1.09	2.31
	Both (n=76)	1.13	1.68
Reimbursement & inventory management		Reimbursement HNS collected vs self	Inventory by HNS vs self
	All handled by HNS (n=106)	1.13	1.92
	Some managed by HNS (n=22)	1.19	2.50
	None managed by HNS (n=16)	2.00	1.97

*HNS=Home Nutrition Service

Appendix A

AMERICAN SOCIETY FOR PARENTERAL AND ENTERAL NUTRITION

STANDARDS
FOR
NUTRITION SUPPORT

Home Patients

January 1985

A.S.P.E.N. is a professional society whose members are health care professionals—physicians, nurses, dietitians, pharmacists and nutritionists—dedicated to optimum nutrition support of patients during hospitalization and rehabilitation.

A.S.P.E.N.'s diverse professional membership reflects the basic importance of good nutrition to good medical practice and the multidiscipline team approach to sound nutrition support.

A.S.P.E.N. has developed these standards to promote the health and welfare of those patients in need of enteral and parenteral nutrition. The standards represent a concensus of A.S.P.E.N.'s members as to that minimal level of care which should be given in order to assure sound and efficient enteral and parenteral nutrition. A.S.P.E.N. disclaims any liability to any health care provider, patient or other persons affected by these standards.

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Dear Colleague:

This publication contains minimal standards of care for home patients to ensure that malnutrition is recognized and effectively and safely treated. The Standards are presented in a format similar to those published for hospitalized patients. Each Standard is usually followed by an explanatory paragraph. Each of these Standards represents minimal acceptable levels of care and should be subscribed to by home health care providers. Specific diagnostic tests, treatment modalities and protocols have not been detailed, but are presented in the broadest, most generic terms so that these can be specified by each patient's home health care provider. These Standards are evolutionary and will be reviewed, updated and amended as needed to keep pace with advancements in medical science and changes in the delivery of health care. The A.S.P.E.N. Committee on Standards, a multidisciplinary group, prepared these final standards after receiving comments on an earlier draft from A.S.P.E.N. members.

We welcome your comments.

Ezra Steiger, M.D.
Chairman, Committee on Standards

STANDARDS FOR HOME NUTRITION SUPPORT

1. Definitions

Enteral nutrition — nutrition provided through or via the gastrointestinal tract
- oral — enteral nutrition taken through or via the mouth
- tube — enteral nutrition provided through a tube that delivers nutrients distal to the oral cavity

Feeding formulation — a ready to administer mixture of nutrients

Home — a patient's residence excluding chronic care and extended care facilities

Malnutrition — any disorder of nutrition, usually a deficiency of nutrient intake or impaired nutrient metabolism

Nutrient — protein, carbohydrate, lipids, vitamins, electrolytes, minerals, and water

Nutrition — the sum of the processes by which one takes in and utilizes nutrients

Nutrition support service — a multidisciplinary group of health care professionals who aid in the provision of specialized nutrition support

Parenteral nutrition — nutrients provided by means other than the gastrointestinal tract
- central — parenteral nutrition delivered through a large diameter vein, usually the subclavian or superior vena cava, that empties directly into the heart
- peripheral — parenteral nutrition delivered through a smaller vein, usually in the hand or forearm

Provider—a physician with expertise in specialized nutrition support who is medically responsible for the patient's home nutrition care

Specialized nutrition assessment — a physician with expertise in specialized nutrition support who is medically responsible for the patient's home nutrition care

Specialized nutrition assessment — a comprehensive approach to defining nutrition status that employs clinical and dietary histories, physical examination, anthropometric measurements, and laboratory data

Specialized nutrition support — provision of specially formulated and/or delivered intravenous or enteral nutrients to prevent or treat malnutrition

Vendor — an organization that supplies equipment and products and provides services to the patient requiring specialized home nutrition support under the direction of the provider

2. Organization

a) PROVIDERS OF SPECIALIZED HOME NUTRITION SUPPORT SERVICES SHALL BE CLEARLY DEFINED.

The provider of specialized home nutrition support is the physician who is primarily responsible for the patient's nutrition care and should be assisted by a registered nurse, a registered dietitian and a registered pharmacist each having appropriate education, specialized training and experience in the discipline of specialized home nutrition support.

Specialized home nutrition support services shall be initiated and coordinated by the provider. There shall be a clear understanding among the provider, the vendor and the patient specifying responsibilities of each including; the manner in which services shall be coordinated and evaluated; the role of the provider, the vendor and the patient in the establishment and monitoring of patient care; and the mechanism and responsibility for payment for services, equipment and products.

b) THE PROVIDERS OF SPECIALIZED HOME NUTRITION SUPPORT SERVICES SHALL BE GUIDED BY WRITTEN POLICIES AND PROCEDURES.

There shall be written policies and procedures concerning the scope and provision of specialized home nutrition support services. These shall be developed by the provider. Concurrence shall be obtained from the medical/surgical, dietetics, nursing, pharmacy and other staff as appropriate. These shall be reviewed annually and revised as appropriate to reflect optimal standards of care. The policies and procedures shall include but not be limited to the following:

1. The roles, responsibilities and 24 hour availability of provider care.
2. Criteria for patient eligibility and selection should be defined. These criteria should include medical suitability; rehabilitative potential; social and economic factors; educable, psychological and emotional factors pertinent to the patient and others who are significantly included in this care.
3. A mechanism for patient monitoring (e.g. frequency of follow-up contact, laboratory studies, and physical examinations).
4. Availability of consultative medical services and services of other professionals such as psychologists and social workers and nonprofessionals, such as patient support groups as appropriate.
5. Reimbursement mechanisms for services, equipment and supplies.
6. Acquisition of enteral or intravenous nutrients, equipment and supplies for home delivery.
7. Educational materials for patient and family training and use at home.
8. Preparation and/or storage of enteral formulas or intravenous nutrient solutions in the home; techniques for the administration of enteral formulas or intravenous nutrient solutions, feeding schedules, care of feeding tubes for patients receiving enteral formulas, and care of catheters and tubing for patients receiving intravenous nutrition.
9. Prevention and management of complications in the home, and emergency consultation with professional staff.
10. Mechanisms for quality assurance.

c) SPECIALIZED HOME NUTRITION SUPPORT SERVICES SHALL BE DOCUMENTED

Medical records shall be maintained for every patient receiving specialized home nutrition support services and shall include:

1. Designation of physician having primary responsibility for the patient's home nutrition care.
2. All pertinent patient diagnoses and prognoses including long and short-term objectives of treatment.
3. Initial and follow-up physical examinations.
4. Scope and results of training and retraining.
5. Plan of care including types and frequency of services to be provided, functional limitations of the patient, activities permitted, psychosocial needs of the patient, suitability and adaptability of the patient's residence for the provision of home nutrition services and name of other individual(s) who will assist in the care of the patient if required.
6. Composition, rate, and mode of administration of feeding formulation and all medications.
7. Signed and dated progress notes for each home visit and clinic visit and telephone contact. These progress notes should include response to therapeutic regimen including results of serial monitoring, complications and revisions in the therapeutic regimen.
8. A summary statement at termination of nutrition therapy which includes results of therapy, complications, outcome and disposition of patient.

d) SPECIALIZED HOME NUTRITION SUPPORT RENDERED SHALL BE REVIEWED AND EVALUATED REGULARLY TO DETERMINE OVERALL EFFECTIVENESS AND SAFETY.

Evaluation of the patient's need for and response to specialized home nutrition support shall be the responsibility of the providers. The review and evaluation shall be performed and documented at least every 90 days. Deficiencies found in the review should be corrected by modifying services, protocols, procedures and educational programs.

3. Patient Selection

a) **Indications and Contraindications for Specialized Home Nutrition Support** — PATIENTS SHALL BE CAREFULLY EVALUATED PRIOR TO SELECTION FOR SPECIALIZED HOME NUTRITION SUPPORT

Candidates for specialized home nutrition support are those patients unable to meet nutrient requirements by oral enteral nutrition. In addition, the patient's clinical status and quality of life must be such that treatment at home would be appropriate. Specialized nutrition support being given at home should be designed to achieve the nutrition objectives. The patient's home environment should be appropriate for the safe use of home nutrition support.

b) **Determination of Nutrition Requirements** — AN EVALUATION OF THE NUTRIENT NEEDS OF THE PATIENT SHALL BE PERFORMED PRIOR TO THE INITIATION OF SPECIALIZED NUTRITION SUPPORT.

Nutrition requirements will be a function of the special disease state, the patient's nutrition status, growth requirements and the duration of anticipated intake. The type and amount of nutrition needed by the patient shall be determined.

4. Therapeutic Plan

a) **Objective** — THE OBJECTIVE(S) OF SPECIALIZED NUTRITION SUPPORT SHALL BE DETERMINED AND DOCUMENTED.

The objectives of home nutrition support should address the short and long term needs of the home patient. Short term needs might include resolution of disease progression, wound healing, progression to enteral support and recovery from nutrition depletion. Long term needs include maintenance of normal nutrition and rehabilitation to physical and social independence. These objectives should be developed prior to the institution of nutrition support.

b) **Mode** — THE ROUTE(S) SELECTED TO PROVIDE SPECIALIZED NUTRITION SUPPORT SHALL BE APPROPRIATE TO MEET ASSESSED NUTRIENT REQUIREMENTS AND ACHIEVE THERAPEUTIC GOALS AND OBJECTIVES.

The safest, most cost effective route which meets the patient's needs should be utilized. The gastrointestinal tract should be used whenever possible. It should be recognized that as the patient's therapy progresses the optimal mode of feeding may change and may, at times, utilize both enteral and parenteral feedings.

c) **Prescription** — THE SELECTED FEEDING FORMULATIONS SHALL BE APPROPRIATE TO THE DISEASE PROCESS, COMPATIBLE WITH THE ACCESS ROUTE, AND MEET NUTRIENT NEEDS.

The formulation selection and modification should be under the direction of the provider and should consider available products and their costs and knowledge of the patient and of his/her specific clinical disease processes. The most cost effective therapy compatible with the access route should be utilized. The patient should be given a prescription copy of the feeding formulation and other medications.

5. Implementation

a) **Establishment of Access**

THE ACCESS ROUTE(S) SHALL BE APPROPRIATE FOR HOME USE.

The type of device used should be placed, recommended or approved by the provider and documented in the patient's medical records. Access should be placed by, or their placement directly supervised by, a physician, nurse or specially trained health care professional who is proficient in their placement. Selected patients or responsible others who have been trained may insert enteral feeding tubes. Standard techniques or protocols should be established for gaining access. The access selected must be appropriate for the type of therapy to be delivered and should be as simple as possible for home care and use, offer appropriate durability for the anticipated duration of therapy, and minimize the potential for occurrence of complications.

b) **Patient Education**

1. THE PATIENT AND/OR RESPONSIBLE OTHER SHALL RECEIVE EDUCATION AND DEMONSTRATE COMPETENCE IN FEEDING FORMULATION PREPARATION AND ADMINISTRATION.

Patients should be educated in the following areas: knowledge of appropriate formulation components, determination of proper dosages, aseptic (parenteral) or clean (enteral) technique, manipulation and maintenance of equipment and infusion method. Patients receiving enteral nutrition must be instructed in clean techniques of feeding formulation preparation, storage and infusion. Closed containers should be used for feeding formulation storage and administration. In general, enteral formulations should not be left hanging for longer than 12 hours but hanging time may be more limited for specific products. Admixed parenteral formulations should not be left at room temperature for longer than 24 hours. Patients receiving parenteral nutrition should be taught to check the integrity of the feeding formulation containers, to inspect for abnormalities in appearance, proper storage of the feeding formulation, and filtering techniques, if used. For cyclic enteral and parenteral infusion methods, specific instruction should be given. Control of the infusion rate to maintain an accurate flow rate requires an infusion control device which the patient or responsible other must be taught to use.

2. THE PATIENT AND/OR RESPONSIBLE OTHER SHALL RECEIVE EDUCATION AND DEMONSTRATE COMPETENCE IN ACCESS ROUTE CARE.

   The patient receiving parenteral infusions must be trained in aseptic technique of dressing care, connecting and disconnecting the intravenous tubing to the catheter and post infusion flushing to prevent catheter occlusion. The enterally fed patient must be trained in clean techniques for handling the tube, maintaining the access site and flushing the tube to maintain patency.

3. THE PATIENT AND/OR RESPONSIBLE OTHER SHALL RECEIVE EDUCATION AND DEMONSTRATE COMPETENCE IN THE RECOGNITION AND APPROPRIATE RESPONSE TO COMPLICATIONS AND EQUIPMENT MAINTENANCE AND MALFUNCTIONS.

   Patients must be taught to recognize and respond to potential complications. However, providers are still responsible for the care of home enteral and parenteral nutrition patients and must be available around the clock to advise and/or intervene if potentially serious complications arise. Common, important clinical complications include sepsis, glucose intolerance, fluid and electrolyte imbalance, catheter or tube occlusion and breakage and equipment malfunction.

4. EDUCATIONAL MATERIALS SHOULD BE PROVIDED TO THE PATIENT OR RESPONSIBLE OTHERS.

5. PATIENT EDUCATION SHALL INCLUDE PERIODIC REASSESSMENT AND RETRAINING AS NEEDED.

6. Patient Monitoring

a) **THE PATIENT SHALL BE MONITORED FOR THERAPEUTIC AND ADVERSE EFFECTS AND CLINICAL CHANGES THAT MAY INFLUENCE SPECIALIZED NUTRITION SUPPORT.**

Protocols should be developed for periodic review of the patient's clinical and biochemical status. Routine monitoring should include nutrient intake; review of current medications; signs of intolerance to therapy; weight changes; biochemical, hematologic and other pertinent data including clinical signs of nutrient deficiencies and excesses as well as adjustment to therapy, changes in lifestyle, psychosocial problems and changes in the home environment. Assessment of the patient's major organ functions should be made periodically.

7. Termination of Therapy

a) **THE PATIENT SHALL DEMONSTRATE THE ABILITY TO INGEST AND ABSORB ADEQUATE NUTRIENTS BY THE ENTERAL ROUTE PRIOR TO DISCONTINUING PARENTERAL NUTRITION.**

Parenteral nutrition should not be discontinued by the provider or vendor until estimated nutrient requirements are tolerated by the gastrointestinal tract. Parenteral nutrient formulations should be decreased over time while enteral feedings are increased. Documentation of ingestion and absorption of adequate nutrients via the gastrointestinal tract should be made in the medical records.

b) **ADEQUATE ORAL ENTERAL NUTRITION SHALL BE DEMONSTRATED PRIOR TO DISCONTINUANCE OF ENTERAL NUTRITION.**

c) SPECIALIZED NUTRITION SUPPORT SHALL BE DISCONTINUED WHEN COMPLICATIONS SO INDICATE.

Complications which are uncontrollable and/or life-threatening require immediate assessment of the patient by the provider physician, and if necessary, immediate discontinuation of the specialized nutrition support therapy. Treating emergent life-threatening conditions takes precedence over the delivery of specialized nutrition support. Specialized nutrition support should be reinstituted following the correction of such complications as indicated.

d) **SPECIALIZED NUTRITION SUPPORT SHALL BE TERMINATED WHEN THE PATIENT NO LONGER BENEFITS FROM THE THERAPY.**

Specialized nutrition support is used in the home setting to prevent starvation and promote an optimum quality of life. When in the course of a patient's disease these objectives can no longer be met, the decision to discontinue specialized nutrition support must be made jointly by the patient, family and provider.

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TASK 5. CONCLUSIONS

The following issues and areas of needed research were developed and prioritized from the material presented in Tasks 1-4 and discussions with the Oley Foundation Scientific Advisory Committee. Consistent with much of the previous material, the issues that impact on the elderly are frequently the most pressing for the therapy as a whole so future investigations in these areas will generally benefit the entire field of nutritional support.

Priority Issues

1. Third-party reimbursement of nutritional support.
2. Establishing the nutritional requirements of the elderly, both enterally and parenterally, in health and disease.
3. Determining the cost effectiveness of nutritional support:
    a) in different disease states;
    b) under both modes of administration.
4. The need for ongoing data collection to evaluate changes in utilization of the technology in both inpatient and outpatient settings.
5. The need to develop mechanisms for disseminating information related to nutrition support research and monitoring its application.

Needed Research

I. As indicated above, a major area for needed research pertains to the economics of nutritional support, both in terms of third-party reimbursement and cost effectiveness* of the therapy. This need holds true for all settings and will be discussed as it relates to each.

A). Hospital Setting: It is clear that nutritional support in hospital patients typically involves the sicker, more debilitated long-stay patient. While there are ICD-9 co-morbidity or complication codes for protein-calorie malnutrition (PCM), as seen in the university hospital study described in Task 2 PCM was only an accompanying diagnosis 30% of the time. In other words, not infrequently and quite appropriately, NS is initiated before PCM has developed. Further since NS is needed for a wide array of conditions, theoretically factoring it into a few specific diagnoses or procedures like "Crohn's disease" or "bowel resection" is untenable. It seems clear that adequate procedure codes for specialized nutrition support procedures need to be developed so they can be factored in as a "severity index" for a broad range of disorders. To ensure that nutritional support is appropriate and not an abused therapy to increase reimbursement, a number of studies are required:

1. Studies which test the cost effectiveness of NS as an adjunct therapy in different disease states, particularly in older patients with limited life expectancy.

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*Cost effectiveness is used in the sense of "what is the least costly way to produce a desired effect or outcome."

2. Studies that determine mechanisms for cost-effective monitoring and proper use of this therapy. In other words, real and needed nutritional support versus token and unnecessary nutritional support. While data exist to show safer and more effective NS[1] in hospitals with a nutritional support team, no study has yet demonstrated that hospitals which develop and underwrite NS teams save money while providing essential NS.

It would be desirable to design studies to see if families and friends, with the advice and supervision of a nutritionist, can stimulate greater oral intake of food by the patient, avoiding the necessity for expensive parenteral or enteral nutrition. In less developed countries such family support, in all aspects of nursing, is very important and mechanisms are developing in the U.S. to limit hospital costs by offering various options for family versus professional nursing care.

3. Parenteral peripheral vein nutritional support (PVNS) can be almost as expensive as parenteral central vein nutritional support (CVNS). PVNS frequently involves less professional decision making. To date there is no academic consensus that PVNS is cost effective. Until such evidence exists, it would seem appropriate to create financial disincentives for such token nutritional support while encouraging necessary nutritional support, either CVNS if required or enteral NS.

4. Studies that evaluate simplifying in-hospital NS to reduce costs, such as use of the "three-in-one" IV solutions (premixed glucose, amino acids and fat); the mixing of a several

liter, 24-hour supply, in one bag; less costly and more reliable infusion pumps; and less expensive, well-tolerated enteral formulas.

B). Nursing Home (NH) Setting: There needs to be further clarification of whether NH nutritional support can truly be separated into adjunctive medical therapy, i.e., treatment of limited duration which can be started or withheld according to medical benefit, in contrast to the hygenic maintenance of patients with chronic disorders, in whom the level of supportive care is more "truly" a societal than a medical decision.

Research needs are:

1. Studies to design simpler, more cost-effective NHNS.

2. Studies to evaluate initiating NS at the NH (e.g., nasogastric tubes placed by nurses, NH percutaneous gastrostomies). What would be the medical indications for such therapy? Does such NHNS avoid a more expensive hospitalization because it prevents the complications of malnutrition, e.g., decubitus ulcers, infections, loss of strength resulting in immobilization?

3. Should parenteral support become more available for NH patients? Currently few nursing homes will accept any patients requiring IV infusions. Is this a safeguard against potential abuse of IVNS or is this an option which should be available to patients and their families for long-term or respite care? It is the personal opinion of some of our consultants that the availability of long-term CVNS could lead to serious abuse of this expensive therapy since the goal of meaningful

rehabilitation would probably be set in only very limited terms. Conversely short-stay respite centers have relevance for families managing older relatives and needing vacations.

C). Home Setting: As shown by data from the Oley Foundation review of HPN, there seem to be two separate groups of patients, a long-term HPN group (chronic, "benign" GI dysfunction) and a short-term HPN group (GI obstruction from a malignancy). Further investigations should determine if it is appropriate to separate these uses by applying different funding mechanisms to underline the differences in training, the complexity of nutrient solution, and the post discharge needs as discussed under Task 4, such as the nursing support needed once home. Thus long-term patients could be funded by the current mechanism, Medicare Part B "prosthetic device," and short-term patients could be funded by Part A "hospice care" or by a DRG-type of mechanism that includes a severity factor determined by including specialized nutrition procedures.

Additional studies should include:

1. Cost-containment studies on the realistic training time and components of home equipment (premix versus homemix, "three-in-one," infusion vests, etc.).

2. Studies on the role of home enteral nutrition versus the more costly home parenteral nutrition. This would include questions on how frequently HEN could be used instead of HPN and does reimbursement promote HPN over HEN. Comparative studies should investigate their relative complication rates, hospital readmissions, and rehabilitative efficacy.

II. A second important research need can be summarized as the evaluation of new developments prior to their widespread use. This seems an obvious requirement and yet throughout medical care generally, improvisation and theoretical benefit have often preceded any clear, scientific cost-effective evaluation. This laissez-faire ambience is probably expensive and unethical and should be replaced by formal testing of medical innovations prior to their widespread dissemination. In the nutritional support arena this requires:

1. Good data collection on new develpments in the use and outcome of NS, such as that information which is to be collected by OASIS.

2. Support for formal testing of new products and their appropriate application, for more information about parenteral versus enteral requirements and how the requirements change with age.

3. Mechanisms for disseminating nutrition support research knowledge and testing for micronutrient levels on a regional basis.

III. A third important need exists in regard to standards of care. What mechanisms are needed in all three settings to ensure quality of care? Technically a vehicle exists for this in the hospital setting by the Joint Commission on Accreditation of Hospitals (JCAH). Thus far the JCAH supervision has not carefully delineated in-hospital standards for NS. Outside the hospital, no general standards exist. As mentioned earlier, ASPEN has provided a baseline for standards of care for home (and hospital) NS and they are currently working on the NH area. However such standards require formal adoption nationwide and credentialing mechanisms to be sure they are upheld.

Notes:

1. Nehme AE: Nutritional support of the hospitalized patient; the team concept. JAMA 243:1906-1908, 1980.

LIFE-SUSTAINING TECHNOLOGIES AND THE ELDERLY
ANTIBIOTICS AND THE ELDERLY

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Task 1 final.doc

David W. Bentley, M.D.

I. Introduction

A. Significance: Decisions regarding interventions with medical technology, e.g., end-stage renal dialysis (ESRD), resuscitation, ventilation, nutritional support and antibiotics, while ultimately made by individual physicians for individual patients, are made in a context that reflects social, ethical, psychological, legal and economic as well as strictly biomedical considerations. Such multi-faceted decision-making has become increasingly common and important in the particular instance of deciding on the use of life-sustaining technologies in the care of elderly patients. The degree to which such decisions reflect a complex mixture of medical and societal considerations has recently been eloquently analyzed for the extreme case of deciding whether or not to provide renal dialysis to elderly patients in Great Britain (Halper, 1985).

Decisions regarding renal dialysis, however, involve a relatively small number of patients and physicians, are made under relatively non-urgent circumstances and with very clear high cost and capital implications. In contrast, decisions regarding antibiotics involve the majority of seriously ill elderly persons and their physicians, and are usually made under urgent circumstances. Antibiotic treatment does not qualify for heroic, or even extraordinary, treatment because it readily available, inexpensive, safe and usually painlessly administered (Brown and Thompson, 1979).

Many physicians, however, forget that many infections in older persons usually represent a complication of a long-term, chronic illness. What is initially perceived as ordinary treatment, e.g., penicillin is "ordinary" for pneumococcal pneumonia, may be extraordinary treatment because the antibiotic only offers to prolong great suffering at extreme costs (Lynn, 1984).

Our assessment of the use of antibiotics in life-sustaining situations in the elderly will be based upon the multi-faceted model in the Figure I-1. Specifically, for each component shown in this model, we shall assemble and analyze relevant information from the existing medical and related literature, as well as from selected current investigations and writings of project participants. Reccomendations will consist of a well-formed set of guidelines on the use of life-sustaining antibiotics for elderly persons in a variety of settings.

B. Definitions

1. Critically ill: Critical illness can be described as "an illness which could lead to imminent death, but might respond to treatment, i.e., pneumonia, pulmonary embolus or myocardial infarction" (Levenson et al, 1981).
2. Terminally ill: Terminal illness can be described as "an illness which will result in imminent death regardless of treatment, i.e., metastatic cancer or certain neurologic disease" (Levenson, et al, 1981).
3. Describe Life-Threatening Infections in General Terms: Life-threatening infections are those infections that require immediate treatment with antibiotics or the patient will die within a day or

two of the onset of the infection. Because it requires 24-48 hours for the pretreatment cultures to demonstrate the bacterial pathogen, these patients must be treated for a presumptive diagnosis and wi antibiotics that are empirically selected. The following specific bacterial infections are generally classified as *life-threatening*: meningitis, septic abortion, or gas gangrene. Septicemia may be associated with any infection and is a clinical term commonly used to describe a bacteremia with clinical manifestations of a severe infection, i.e., chills, fever, malaise, toxicity and hypotension. Generalized overwhelming sepsis is fever or hypothermia (< 97 F), hypotension and confusion or delerium. These conditions are associated with high mortality rates and require prompt diagnostic efforts and rapid effective treatment. Immunocompromised patients, including patients with leukemia and those receiving cancer chemotherapy, who are *moderately ill with focal infections* such as pneumonia or urinary tract infections, also require immediate therapy. Elderly patients are also included in this last group because of the high morbidity and mortality rates following such infections.

3. *Describe Life-Threatening in Terms of Specific Infections*: *Bacterial pneumonia* is considered life-threatening for older patients when there are signs of septicemia or overwhelming sepsis or specific pneumonia-associated findings that correlate with increased mortality rates, e.g., involvement of two or more lobes of the lung, a leukocyte count < 5000 cells/mm^3 or an extrapulmonary focus (Austrian and Gold, 1964).

Urinary tract infections are considered life-threatening when there are signs of septicemia or overwhelming sepsis.

Infected decubiti are considered life-threatening when there are signs of septicemia, overwhelming sepsis, rapidly spreading cellulitis (acute inflammation of the skin and subcutaneous tissues by bacteria, frequently anaerobic (gas-producing) bacteria), or gas gangrene.

Total parenteral nutrition-associated septicemia is considered life-threatening when there are signs of septicemia or overwhelming sepsis. It is important to note that any local infection in an elderly patient can rapidly lead to overwhelming sepsis. Therefore, all elderly patients have potentially life-threatening infections which means that older persons who are mildly ill with focal infections, must be treated promptly to avoid undue complications.

Task I. Describe Current Treatment Practices

I. Background on Specific Infections Reviewed

A. Bacterial Pneumonia: Bacterial pneumonia is probably the most important infection of older persons because it occurs frequently and with increased morbidity and mortality. Pneumonia (and influenza) is the fourth leading cause of death in the United States population 65 years of age and older, accounting for 184.8 deaths per 100,000 persons (Kovar, 1973). Mortality rates range from 10% to 40% for pneumonias due to organisms causing minimal lung destruction (e.g., *Streptococcus pneumoniae* (Hook et al, 1983) to as high as 80% for pneumonias due to Staphylococcus aureus or gram-negative bacilli that frequently cause necrosis of the lung (Sullivan et al, 1972).

Bacterial pneumonia in older persons occurs following oropharyngeal colonization with respiratory pathogens, aspiration of these pathogens or normal flora alone, and impaired clearance of these bacteria-laden oropharyngeal secretions by the lung. Several possible predisposing age-associated factors include: 1) increased oropharyngeal colonization rates by gram-negative bacilli and S. aureus, 2) increased silent aspiration, 3) decreased effective cough and mucociliary transport mechanisms, 4) possible intrinsic defects in alveolar macrophages and polymorphonuclear leukocytes and 5) an unknown role of impaired T-cell function. In addition, several disease or condition-associated factors that predispose to pneumonia are more frequent or affect the elderly more severely such as chronic bronchitis, congestive heart failure, cerebral vascular accidents and dementia (Bentley, 1986).

B. Urinary Tract Infection: The urinary tract is the most frequent site of bacterial infection in older persons. The vast majority of UTI's in the elderly as asymptomatic, but much controversy exists regarding the natural history of the bacteriuria. Some reports demonstrate an increased association with renal dysfunction and hypertension with bacteriuria (Marketos & Dontas, 1970; Marketos et al, 1969) whereas others do not (Aktar et al, 1972; Nicolle et al, 1983). All agree that bacteriuria, especially in association with obstructive uropathies and instrumentation, can be a serious problem for older persons. Approximately 55% of community-acquired and nosocomial gram-negative bacteremias occur in persons over 65 years of age and UTI's, with or without genitourinary manipulation are the source of 33% of these cases (Kreger et al, 1980).

Normally, the urinary tract is free of urinary pathogens. The reason(s) that UTI's are so frequent in older persons is unknown, but several factors may be responsible. In men, they include increased residual urine and obstructive uropathy secondary to benign prostatic hypertrophy with subsequent instrumentation and surgery, chronic prostatitis caused by age-associated prostatic microcalculi and possible alterations in normal bactericidal characteristics of the prostatic secretions. In women, they include residual urine secondary to loss of pelvic support, contamination of the perineum, which is increased with fecal incontinence and possible loss of local bladder mucosal defense mechanisms secondary to decreased local antibody and/or epithelialization of portions of the bladder mucosa associated with menopause (Brocklehurst, 1971; Kaye, 1980).

C. Infected Decubiti (Pressure Sores): The term, decubitus ulcer, is derived from the Latin "decub" meaning lying down. Because a large percent of these sores occur in the sitting and other positions, where pressure, shearing forces, friction and moisture lead to tissue necrosis, the term "pressure sore" should be used because it is more accurate and describes the underlying pathophysiology (Reuler and Cooney, 1981).

Infected pressure sores are the result of local infection of the full-thickness of the ulcer stage with aerobic and anaerobic bacteria that results in a deep pressure sore with necrosis extending to and through the deep fascia. This is often a life-threatening lesion with associated septicemia, but there have been few studies that have addressed this problem systematically (see section V). In an investigation of 24 patients who required antibiotic treatment for sepsis attributed to to a pressure sore, positive blood cultures were documented in 19 (79%) of the patients (Chow et al, 1977).

Elderly patients with pressure sores associated with bacteremia have a very poor prognosis. The mortality rates for this complication in the series noted were the highest (76%) in elderly patients compared to a mortality rate of 13% in patients < 60 years of age (Chow et al, 1977).

Penetration of the deep fascia by the infected necrotic process allows extensive spread to adjacent tissues. Contiguous spread to underlying bone and the development of osteomyelitis is frequent and can be documented in up to 40% of cases (Chow et al, 1977). Sinus tracts may extend to adjacent join (pyoarthrosis) or to deeper structures leading to bladder or bowel fistule.

D. Iatrogenic Infections: The iatrogenic infections are infections that result from diagnostic or therapeutic maneuvers employed in the management of an acute or chronic illness. The iatrogenic infections, which result from the use of life-sustaining technologies, are caused by medical devices, which are defined as any foreign body placed temporarily or semipermanently in a patient's tissue for diagnostic or therapeutic pruposes (Stamm, 1978). In the late 1970's it was estimated that there were more than 850,000 device-related infections, accounting for approximately 45% of all nosocomial infections that occurred in the United States (Stamm, 1978). The iatrogenic infections resulting from the use of life-sustaining technologies, such as nutritional support equipment, e.g., peripheral alimentation via plastic catheters and total parenteral nutrition, mechanical ventilators and hemodialysis machines form a substantial proportion of these iatrogenic complications (Table I . 2).

Although the risk of infection associated with most medical devices has been fairly well described, we could find no information on age-specific rates of infection to determine the number of elderly patients who have experienced these infections (Haley, 1981; Gross et al, 1983). Conservative estimates of national usage suggest that at least 16.8 million medical devices were used in hospitals in the United States in the late 1970's (Stamm, 1978). The calculations in Table I . 2 were based on an estimated 38 million acute-care admissions annually times percent of hospitalized patients with each device times estimated reate of device-associated infection. If the total number of medicare-reimbursed admissions, i.e., patients 65+ years of age, is obtained and the percent of 38 million calculated, the estimated number of annual cases of device-related infections in elderly hospitalized patients can be calculated from Table I . 2 . (see numbers in parentheses). This assumes that there is a proportionate rate of hospitalized elderly patients with each device and a proportionate rate of device-associated infections in elderly patients-both assumptions probably underestimate the true picture.

In our proposal (page 4) we indicated that we would assess bacteremia associated with hemodialysis as an example of an iatrogenic infection afflicting the elderly. This was based on an assumption that there would be available already summarized data from the Monroe Community Hospital-based Hemodialysis Unit, which prior to its transfer to another site in January 1985, cared for a large number of older patients. After much careful searching, however, this data could not be located and the financial and time constraints of the subcontract prevents further efforts here.

In this report we will discuss, instead, septicemia associated with nutritional support equipment. Nutritional support is provided by several different methods. Enteral alimentation, which requires nasogastric tube or gastrostomy or jejunostomy tubes, is seldom associated with bacteremia and life-threatening infections (Heynsfield et al, 1979), although contamination of the infusion device occurs (Anderton, 1983). Peripheral parenteral alimentation has been used sparingly. This device employs an indwelling plastic catheter inserted into a peripheral vein; the attendant risk of sepsis are similar to those associated with other uses of these devices (Stamm, 1978; Chipponi et al, 1981). for this report, therefore, we have focused on total parenteral nutrition (TPN) as the nutritional support equipment for discussion.

Several aspects of the delivery of TPN increase the risk of bacteremia or fungemia (invasion of the bloodstream by fungus) and separates this mode of therapy from other treatments requiring peripheral or central intravascular catheters (Henderson, 1985). They include:

1. The composition of the infusate supports the growth of different microorganisms, including Candida species.
2. The hypertoneity of the solution tends to cause thrombosis resulting in increased risk of infection.
3. TPN catheters remain in place much longer leading to increased problems with catheter contamination and
4. Elderly patients requiring TPN are frequently severly ill due to neoplasmas, trauma, etc., with increased risk of bacteremia and hematogenous seeding of the catheter.

TPN-associated septicemia is defined as the isolation of the same organism from the catheter and from the blood plus no clinical (or autopsy) and microbiologic data suggesting any other source of infection. It is caused by microbial contamination during the infusion therapy. The pathogens may gain access to the system at several sites (Figure I.3) but the most frequent point of entry is the site at which the device penetrates the skin (Henderson, 1985).

A number of patient-related risk factors, including being > 60 years old (Maki 1981), have been associated with an increased risk of device-associated bacteremia (Table I.4) but unable to locate primary source. A recent prospective risk-factor analysis of TPN-associated infections, however, noted that there was no relationship with age (Table I.5, Snydman et al, 1982). The number of infected cases (12), however, was very small and these findings, therefore, must await a larger series that includes more older persons.

II. Influences of Setting on Four Specific Infections

A. Bacterial Pneumonia: Bacterial pneumonia occurs in several different settings, e.g., community, institution (nursing home or other long-term care facility) or hospital. Although there are only limited studies to date, it is likely that each setting, plus associated host conditions, predispose to different etiologic agents (Bentley et al, 1981; Ebright & Rytel, 1978; Verghese & Berk, 1983). The estimated prevalence of etiologic agents causing pneumonia in the elderly in these settings is presented in Table I.6.

B. Urinary Tract Infections: The etiologic agents causing UTI's in the elderly depend on the setting and associated factors, including disease, disability and other conditions such as antibiotic usage and the presence of indwelling bladder catheters (IDBC's). The estimated prevalence of etiologic agents causing UTI's in the community, institution and hospital are summarized in Table I.7.

C. Infected Pressure Sores: The necrotizing infection associated with pressures in a polymicrobial bacterial infection due primarily to the patients own skin and bowel flora. Thus the etiologic agents are similar regardless of the setting. Table I.8 summarizes the microbiology of the infected pressure sores and the associated bacteremia in a small series of 21 patients (Galpin, 1976). Only a few other studies are available (Chow & Burdge, 1983), and they demonstrate similar findings.

D. TPN-Associated Septicemia: In numerous studies, Candida, a fungus, is the principal pathogen causing TPN-associated septicemia in hospitalized patients (Table 1 . 9 ; Goldman & Maki, 1973). Other pathogens isolated from the blood include Staphylococcus aureus, Staphylococcus epidermidis and occasionally gram-negative bacilli (Dillon et al, 1973; Snydman et al, 1982). Most of the Candida infections are probably the result of contamination of the skin at the catheter site.

Hospitalized-associated risk factors promoting colonization of the gut and skin with Candida include multiple antibiotic therapy, prolonged intravenous infusions, corticosteroid or other immunosuppressive therapy and surgical procedures. In the absence of these risk factors, S. aureus has been reported as a sole pathogen causing septicemia associated with right atrial catheterization for prolonged parenteral nutrition at home (Riella & Scribner, 1976).

We have identified no source that documents the influence of the hospice on these four specific infections.

III. Information Available on Decade-specific Risk of Four Specific Infections.

A. Review of the Literature

1. Bacterial Pneumonia: No information could be found on decade-specific risk for this infection

2. Urinary Tract Infections: No information could be found on decade-specific risk for this infection

3. Infected Pressure Sores: No information could be found on decade-specific risk of infected pressure sores. Indirect estimates, however, can be made from a recent survey of pressure sores in Glasgow Scotland (Barbenel et al, 1977; Table 1.10). Older patients had a nearly two-fold increase in the risk of grade

4 pressure sores severe enough to be highly susceptible to life-threatening infections, i.e., 1.7% for persons 60+ years of age vs. 0.9% for persons 20-49 years of age. There was no appreciable difference in the rates of severe pressure sores in persons 70 years of age and older who accounted for 70% of the total patients with pressure sores in spite of representing only 8.4% of the total population.

4. TPN-associated Septicemia: No information could be found on decade-specific risk for this infection.

IV. Other Patient Factors Affecting Treatment Practices for Specific Infections in Specific Settings

This material is found in Task II and the Supplemental Proposal, Psychosocial Variables as Predictors of Treatment Choice in Elderly Nursing Home Residents.

V. Incidence and Prevalence of Specific Infections in Special Settings

A. Review of the Literature

B. Bacterial Pneumonia: The incidence of community-acquired bacterial pneumonia in older persons in the United States ranges from 20 per 1,000 per year in low-risk persons (Kaiser-Permanente Clinic Patients) to 40 per 1,000 per year in high-risk persons (native Americans on reservations), (Fried, 1978; Oseasohn, 1978). Garibaldi and colleagues (1981) conducted a series of 1-day prevalence surveys in 7 Salt Lake City Skilled-Care Nursing Homes, lower respiratory tract infections, primarily pneumonias, were noted in 11 (2.1%) of the 532 patients surveyed. The rates of institution-acquired pneumonia may be as high as 70-115 per 1,000 per year for older persons so disabled that they must be cared for in a public chronic disease hospital (Bentley, 1981). The incidence of hospital-acquired bacterial pneumonia for persons admitted to non-federal acute hospitals is approximately 8.5 per 1,000 admissions per year; the rate for persons over 65 years of age is approximately 17 per 1,000 admissions per year (Haley, 1981). We have identified no source that documents the incidence or prevalence of life-threatening pneumonias in older persons.

2. Urinary Tract Infection: The prevalence of UTI's increases with age, level of care and decreasing fuctional capacity Table I.10; Kaye, 1980). We have identified no source that documents the incidence or prevalence of life-threatening UTI's in older persons.

3. Infected Pressure Sores: Although the association of pressure sores with bacteremia is now well-established (Bryan et al, 1983), there is little information on the incidence or prevalence of life-threatening infected pressure sores in older persons. Peromet et al (1973), studied prospectively 27 patients with pressure sores; bacteremia was observed in 6 (22%) of the patients. Bryan et al (1983), studied 104 episodes of bacteremia in 102 patients with pressure sores over 5 years in 4 hospitals in Columbia, South Carolina. This is an incidence of 3.46 episodes per 1,000 patient discharges. Based on strict criteria, pressure sores were considered the "probable" source of the bacteremia in 49% of the episodes. Another site of infection was also documented in 50% of these

patients indicating that multiple sites of infection are frequently present in hospitalized patients with pressure sores. Unfortunately, no attempt was made to determine the prevalence of pressure sores in the four hospitals and the report gives no information on the age distributions of the patients. Garibaldi and colleagues (1981) noted that infected pressure sores were the leading cause of infection accounting for 32 (6.0%) infections among the 532 nursing home patients studied.

In a study from Glasgow, Scotland (Baribenel et al, 1977, Table I.11), approximately 9% of elderly patients, who were studied in both hospital and community settings, had at least one pressure sore for an incidence of approximately 86 per 100,000 per persons per year. Of these, approximately 1.7% of patients 60+ years of age had pressure sores highly susceptible to life-threatening infections, i.e., destruction of the skin with ulceration. If 20% sustained a life-threatening infection (the actual prevalence is unknown), the incidence of this complication would have been approximately 0.3 per 100,000 older persons per year.

4. TPN-associated Septicemia: With formal infection control practices in place, the prevalence of septicemia in approximately 2,000 hospitalized patients receiving TPN is approximately 7% (Table I.9; Goldmann & Maki, 1973). More recently, a prospective study of 69 hospitalized patients receiving 100 courses of TPN

documented 12 (12%) infections: 5 (5%) with septicemia and 7 (7%) with local canula-related infections (Snydman et al, 1982). Newer catheters, e.g., silicon rubber catheters (Broviac or Hickman Catheters), are inserted via a subcutaneous tunnel for use as chronic indwelling right atrial catheters and are associated with approximately one episode of septicemia per 5.5 patient-years in hospitalized patients (Blacklock et al, 1980). This is the same rate noted in ambulatory patients receiving prolonged TPN at home (Riella & Scribner, 1976). We have identified no source that documents the incidence or prevalence of life-threatening TPN-associated septicemia in older persons in either setting.

No information could be found on the incidence or prevalence of specific infections in hospices.

B. Community Estimates from National Ambulatory Medicine Care Study (NAMCS), NCHS

Additional information on estimates of community-acquired bacterial pneumonia, urinary tract infections (UTI's) and decubitus ulcers were obtained from the NAMCS (Table 1.12 a-c). No cases were identified of TPN-associated septicemia.

VI. Laboratory Tests for Definitive Diagnosis of Specific Infections in Special Settings

A. Review of the Literature

1. Bacterial Pneumonia

Non-invasive (ordinary effort) tests include a new infiltrate on chest x-ray compatible with pneumonia and a culture of the best available secretion from the lower respiratory tract demonstrating lower respiratory pathogen(s). A blood culture, requires a venapuncture but is considered an ordinary effort. It is often the definitive diagnostic test when it demonstrates a respiratory pathogen, e.g., *S*. *Pneumoniae*, *H*. *influenzae*, *Klebsiella* species, etc., and no other suspicious site is identified. These tests are readily available in the hospital, less frequently employed in elderly patients in nursing homes and even less frequently employed in the diagnosis of community-acquired pneumonia unless the elderly patient is seen in the office or hospital-based emergency room.

Invasive (extraordinary effort) tests include thoracentesis, a percutaneous needle aspiration of any fluid in the pleural space surrounding the lung. Transtracheal aspiration (TTA) requires puncture of of the cricothyroid membrane following antiseptic cleaning of the skin and local anesthetic which dulls the pain caused by inserting the needle with an enclosed plastic catheter. Many consider that TTA's are too dangerous to be used in older patients (Rozas & Goldman, 1982). Physicians, in general, are uncomfortable about the procedure because the needle is inserted just below the vocal cords in the larynx and, for this reason, this procedure is infrequently used with older persons. Other studies (Berk et al, 1981), however, suggest that TTA is a safe and useful procedure in the management of bacterial pneumonia, especially in severely ill and hospitalized elderly patients. More complicated (and hazardous) invasive procedures include percutaneous transthoracic lung aspiration and fiberoptic bronchoscopy with protected bacteriologic specimen brush, but these are used infrequently except in immunocompromised patients.

2. Urinary Tract Infections: Noninvasive tests include the demonstration of bacteria on the microscopic examination of an unspun urine and a urine culture that demonstrates more than 10,000 bacteria/ml. A blood culture can be a definitive diagnostic test when it demonstrates the same pathogen noted in the urine, e.g., *E. coli*, *Klebsiella* species, *Proteus* species, *Ps.* aerugenosa, etc., and no other specific site is identified. When it is important to diagnose the etiologic agent without delay, a single catheterization with the smallest catheter available and careful technique is frequently employed, especially in frail or bedridden elderly women.

3. Infected Pressure Sores: Noninvasive tests, such as swabbing the ulcer surface to obtain a culture, is of little value because this approach does not distinguish between bacterial colonization vs. pathogens invading the deeper tissue. Invasive (ordinary effort) tests for culture include needle aspiration through normal intact skin at the edge of the ulcer or cellulitis to obtain tissue juices (Uman & Kunin, 1975).

Invasive (extraordinary effort) tests include fine-needle aspiration biopsy (Lee et al, 1985) or quanitative bacterial cultures of deep tissue from biopsy specimens at the time of surgical debridement. Plan x-rays of the bones and radionuclice imaging studies, e.g., technitium^{99} and gallium^{67} scans, are often obtained to diagnose osteomyelitis. But the diagnosis is often difficult because these tests may give false-positive results. Therefore, more invasive procedures are usually required. Bone biopsy for histologic examination is frequently necessary to make the diagnosis; biopsy for culture is usually necessary to identify the etiologic agent(s). Sinograms, infusion of radiopaque dye through a fistula, are frequently performed to delineate the extent of the sinus tract extending to distant soft tissue structures.

4. TPN-associated Septicemia: Noninvasive (ordinary effort) tests include cultures of the catheter and blood. If septicemia is suspected and the catheter is left in place, quantitative blood cultures are obtained by drawing blood back through the putitively contaminated catheter and the results are compared with quantitative blood cultures obtained via a peripheral vein from an extremity not involved in the infusion (Wing et al, 1979; Felces et al, 1979). If the catheter is removed, a semiquantitative culture technique of the catheter is employed (Maki et al, 1977). No invasive (extraordinary) diagnostic tests are required.

B. Proportion of Infective Episodes with Laboratory Tests Pretreatment: We could find no information on the proportion of life-threatening episodes of four specific infections in older patients that had pretreatment laboratory tests. In one retrospective review of 5, 288 in 20 hospitals that were randomly selected from 194 general hospitals in Pennsylvania, 65% of antibiotic courses initiated for an infectious disease had at least one culture taken in association with the initiation of the course (Shapiro et al, 1979). In a 100-bed, level-III proprietary nursing home over a four-year period, 11% of the patients for whom antibiotics were prescribed had pretreatment bacteriologic studies (Howard et al, 1978). Brown & Thomson (1979) noted that laboratory and x-ray tests were performed in 43 of 190 (23%) patients with febrile episodes, including 38 of 109 (35%) treated patients and 51 of 81 (6%) untreated patients. Recent studies by our group (Zimmer et al, 1985) come closest to answering the question but did not specifically identify life-threatening infections. [see page 22 for details on population study] We noted that pretreatment laboratory studies were ordered in 66 of 173 (38%) nursing home residents with suspected infections. This included 8 (25%) chest x-rays and 1 (3%) sputum culture in the 33 patients with suspected pneumonia and 24 (24%) urinalyses and 56 (57%) urine cultures in the 101 patients with suspected UTI's. The difficulty in obtaining satisfactory chest x-rays and respiratory secretions in nursing home patients with pneumonia probably accounts for the substantial reduction in pretreatment laboratory tests in these patients whereas urinalyses and urine cultures are much easier to obtain in patients with UTI's.

Information is not available in this study on infected pressure sores and there were no patients with TPN-associated septicemia.

The above findings, are limited but suggest that in the hospital setting, where laboratory support is readily available and its use is "expected", laboratory tests are frequently used pretreatment. In nursing homes, however, the converse is true. There is little information on the community setting, but surely pretreatment laboratory testing is even less frequently used here

The general guidelines for characterizing infections in the hospice setting (Calman, 1976) note that asymptomatic infection requires no investigation. But because infection causing severe symptoms should usually be treated, isolation of organisms and determination of their antibiotic sensitivities will be done in the usual way.

VII. Utilization and Expenditure for Antibiotic Treatment of Four Specific Infections in Special Settings

A. Review of Literature

1. Choice of antibiotics, dose and frequency, route of administration and duration.

a. Usual practice employed by practitioners: We have not identified in the literature reports tabulating the current usual treatment practices regarding the specific choice of antibiotics for each of the four specific life-threatening infections in older patients in the various settings. The following generalization, however, can be made:

1) In the community: oral antibiotics are used almost exclusively except occasionally for an initial injection at the end of the office visit and just prior to sending the patient home (not life-threatening infection) or to the hospital. These practices are similar for all patients, including older persons.

2) In the nursing home: the practice is to use oral antibiotics initially for mild to moderately severe infections. If the resident/patient recovers, oral treatment is continued for the duration of the course. If he/she worsens, or if the specific infection presents as a serious or life-threatening disease, the resident/patient is transferred promptly to an acute hospital. Parenteral antibiotics are rarely used in this setting because of

the lack of availability of on-site pharmacist for admixing, i.e., mixing sterile antibiotic powder in the manufacturers vial with diluent, difficulty in providing unit-dosing and the limited number of authorized on-site personnel to give injections of infusions.

3) In the hospital: The practice is to use parenteral (IM or IV) antibiotics until an obvious clinical response occurs, e.g., the patient loses all signs of toxicity and becomes afebrile. Following this, the dose (and route) of the antibiotic is frequently changed to IM or PO to avoid unnecessary complications of prolonged IV's, especially septic complications associated with indwelling venous catheters.

4) In the hospice: The practice is similar to the community and the nursing home except that the emphasis is primarily on using antibiotics to make the patient comfortable and improve his/her quality of life (Baines, 1978) . Oral antibiotics are employed almost exclusively to avoid the added discomfort of i.m. injections. Information from our personal experience is noted in Task I sections VII A2 and VII D (nursing homes) and in the recommendations section below. Additional information on the usual choice of antibiotics by practitioners may be available when the final reports are received from several agencies, including: NAMCS, National Ambulatory Medical Care Survey (community); Health Information Designs (nursing homes) and IMS, America Ltd., National Disease and Therapeutic Index (community and hospital).

b. Recommendations: The pharmacokinetics of several classes of drugs have been studied in older persons which has allowed generalizations concerning alterations in absorption, distribution metabolism and excretion of antibiotics in this high-risk population (DeTorres & Marr, 1983; Gallis, 1984; Lamy, 1984). These alterations, however, depend primarily on co-existing abnormalities in liver and/or renal function; there is little information on whether the pharmacokinetics of antibiotics are altered in healthy older persons. Moreover, an understanding these alterations, which ise required to reduce adverse reactions, are important primarily in long-term treatment of chronic infections. Although there are several concerns (see OTA Chapter 9, pages 46-47), there are no studies that document that antibiotics may be less effective in treating infections in older patients. Thus, the use of antibiotics for life-threatening infections in older patients requires maximum recommended dosages for any adult, except in the presence of obvious liver or renal dysfunction, and an optimal duration of treatment.

Initial therapy for life-threatening infections in older patients is always selected empirically before the culture results are available. The choice of antibiotic is based on the usual pathogen(s) involved which is frequently influenced by the setting in which the infection occurs. The recommended maximum daily dose, as cited in Tables I.13-I.15a and I.15b, is from an authoritative textbook of infectious diseases (Norris and Mandel, 1985). The recommended minimum duration (days) is an "average" duration based on the author's personal experience (Bentley, 1986).

1) Recommended first choice antibiotics and alternatives for *bacterial pneumonia* in the elderly has been identified using the estimated prevalence of etiologic agents causing pneumonia in the elderly according to the setting (Bentley, 1984; Rozas and Goldman, 1982). The list of antibiotics in Table I.13 for *life-threatening* pneumonias in the elderly represents the author's current views which are supported by a recent report on the treatment of pneumonia in adults (Donowitz & Mandell, 1983).

Approximately 80% of community-acquired pneumonias are caused by the *S. pneumoniae* and mixed flora which respond to relatively simple, inexpensive antibiotics with reduced toxicity, e.g., penicillin G, ampicillin or first or second generation cephalosporins (Bentley, 1986). But the increasing frequency of gram-negative bacillary pneumonias, in community-residing elderly, and the associated increase in mortality rates, warrants appropriate empiric treatment for life-threatening situation. The regimen currently favored includes a third-generation cehphalosporin and an aminoglycoside. Future studies may demonstrate the efficacy of the less toxic regimen of a third-generation cephalosporin alone in this setting where a psuedomonas pneumonia is uncommon. Chloramphenicol is an alternative drug for patients with a history of anaphylactic reaction or interstitial nephritis from either a penicillin or cephalosporin and is the drug of choice when *H. influenza* is suspected in an older patient with a life-threatening pneumonia.

2) Specific antibiotics for initial empiric therapy for community-, institution- and hospital-acquired *life-threatening UTIs* in older patients, i.e., pylonephritis and septicemia associated with any site (bladder, prostate, etc.) have been recommended (Gleckman et al, 1982; Kaye, 1980; Sherman et al, 1980) and are summarized in Table I.14. Older persons, who are in the community, should be hospitalized because bacteremia and septic shock occur more frequently than in younger persons (Gleckman et al, 1982). Regardless of the setting, e.g., community, institution, or hospital, initial empiric antibiotic treatment should be with a parenteral broad-spectrum antibiotic regimen with bactericidal activity for *Ps. aeruginosa* because 1) unlike younger persons, *E. coli* accounts for < 50% of UTIs in the elderly, even for community-acquired episodes, 2) the gram stain assessment of the urine cannot distinguish between members of the Enterobacteriaceae family, e.g., that are usually *Proteus sp.*, *Klebsiella sp.*, etc., and *Ps. aeruginosa* and 3) *Ps. aeruginosa* must be considered with the predisposing conditions frequently present (Kreger et al, 1980).

The regimen most frequently recommended for this syndrome is an aminoglycoside that is effective against pseudomonas plus parenteral ampicillin (Ronald, 1984). This is appropriate for UTIs due to gram-negative bacilli and enterococci; vancomycin should be substituted for ampicillin in the penicillin-allergic patient when the Gram stain of the urine suggests enterococcal or staphlococcal UTI. In this case the combined side effects of vancomycin and the aminoglycoside should be monitored closely to avoid the increased risk of oto- and renal toxicity. Newer widespectrum antibiotic agents, e.g., as the third-generation cephalosporins or the fourth-generation penicillins, may be as effective when used as single agents in the initial treatment of complicated UTI (Gillenwater, 1983; Ronald 1984). For the present, however, these drugs should be considered when the sensitivity tests are available.

3) The role of antibiotics in life-threatening *infected pressure* sores is to treat associated cellulitis, high fever, or suspected septicemia. Because the etiologic bacterial agents are usually mixed aerobes (gram-negative bacilli, including *Ps. aeruginosa* and *S. aureus*) and anaerobes (*B. fragilus* and anaerobic streptococci), it is necessary to start antibiotics targeted for these pathogens before culture results are available. Specific regimens for empiric therapy have been recommended (Chow & Burdge, 1983) and are summmarized in Table I.15a. These antibiotics must be administered IV and in high doses to ensure adequate penetration into ischemic and necrotic soft tissues. Bacteria, however, may persist in deep-seated infections unless early and complete surgical removal of necrotic tissue is performed.

The role of surgical intervention cannot be over emphasized (Chow et al, 1977). Even with appropriate antibiotic therapy, significantly higher mortality rates are noted in patients without surgical intervention (67%, 4 of 6 patients) than in those who have surgery in addition to antibiotics (14%, 2 of 14 patients). The fact that bacteremia often persists, even in the presence of effective treatment, but clears promptly after surgical debridement, further atests to the importance of surgical intervention.

4) Specific antibiotics for initial empiric therapy for TPN-associated septicemia are directed primarily against *S. aureus*, *S. epidermidis* and gram-negative bacilli (Table I.15b) Although the septicemia associated with TPN rapidly resolves, in nearly all cases, once the infected catheter is removed (Ryan et al, 1974), antibiotics are always used in older persons once the diagnosis of a septicemic-like picture becomes evident. If the septicemia is associated with TPN the duration of treatment can frequently be reduced by nearly one-third to one-half, or approximately seven days. Unless there is evidence of serious local infection, i.e., septic thrombophlebitis, a distal septic focus or the bacteremia continues once the catheter is removed. A 5-7 day course of amphotericin B is given if the fungemia persists. The catheter is removed if there is no other source of sepsis in the bacteremia or fungemia continues, or in any patient with septic shock (Ryan et al, 1974).

There is another major reason for the prompt and effective use of antibiotics in older persons with septicemia while receiving TPN. In approximately 75% of episodes of septicemia occuring in hospitalized patients (14 of 19) receiving TPN, there is evidence of a septic focus in another anatomic site (Dillon et al, 1973). Elderly patients in this setting are generally malnourished and suffering from major medical diseases or surgical complications that pose a substantial risk for the development of new infections. Serious infections, such as postoperative infected wounds, pneumonia, UTI or intraabdominal abcesses, are frequently associated with septicemia due to a wide variety of gram-negative bacilli. These infections must be treated with appropriate antibiotic regimens. Hyperalimentation can be continued during this antibiotic treatment because hematogenous seeding of the catheter from these distant sites is infrequent (Ryan et al, 1974).

The optimum duration of treatment of the various life-threatening infections is unknown and is difficult to list. Therefore, the recommended minimum duration of treatment was selected for this discussion but there are problems because the duration of treatment depends on multiple factors. Some of these factors, such as etiologic agent(s) are identified early in the course of treatment. If S. pneumoniae was identified as the etiologic agent in a case of bacterial pneumonia, the duration of treatment might be as short as 7 days. Pneumonias due to gram-negative bacilli, however, would be treated for a minimum of 14 days. Complications such as necrosis of the lung or empyema (pus in the pleural space) often requires an additional 1-2 weeks of treatment. In Table I.13, we have arbitrarily considered that the community-acquired pneumonias are caused by S. pneumoniae whereas the institution and hospital acquired pneumonias were caused by gram-negative bacilli without added necrosis or other complications which might warrant a 3-4 week course.

The recommended minimum duration of treatment for life-threatening UTI's in older persons is 14 days (Bentley, 1986) but frequently by 4-5 days there is a response to the empirically selected parenteral antibiotics with elimination of the bacteriuria and loss of fever. At this time, the most appropriate orally administered antibiotic is selected based on sensitivity results and continued for a total course of 14 days. Similar decisions play a role in determining the duration of treatment for life-threatening pressure sores, e.g., extensive surgical debridement, and TPN-associated septicemia, e.g., removal of the venous catheter and prompt clearing of the bacteremia, which shortens the course of initially selected high dose parenteral antibiotics.

The recommended miminum duration of treatment in Tables I.13 to I.15 was selected as a "average" minimum duration (days) of treatment with the high-dose parenteral antibiotics only. It was assumed that there will be no change to a simpler less costly regimen, including oral antibiotics, to avoid further difficulties in identifying a standard of treatment and, therefore, a standard cost of treatment.

2. Documentation of Antibiotic Use

a. Hospitals. The rationale for starting antibiotics is usually evident in hospital settings because of extensive required daily progress notes by multiple caregivers, although there is much variability. Of 2,136 antibiotics single-group courses, e.g., cephalosporins, in patients in 20 randomly selected hospitals in Pennsylvania, only for 57 (3%) were the reason for initiation unknown or could not be interpreted from the information available in the chart (Shapiro et al, 1979; I.16 [Table 7]). In another study of antibiotic use in a large (464-bed) private community hospital (Stevens et al, 1981), however, no explanation for antibiotic use or acknowledgement of the presence of infection was found in 26 (35%) of the 75 patients receiving drugs judged as therapy.

b. Nursing Homes (Summary of MCH-UR Materials)

Dr. Bentley and colleagues (Zimmer et al, 1986) recently studied the use of antibiotics in nursing homes in the Monroe County area. In this evaluation of the prevalence and quality of systemic antibiotic use in nursing homes, we surveyed 42 skilled nursing (SNFs) and their 11 attached intermediate care facilities (ICFs). A random sample of 2238 patients (51%) from the total of 4378 beds was selected and of these, 173 patients (7.7%), including 8.6% of the SNF and 4.5% of the ICF patients) were on systemic antibiotics on the day of the survey. The characteristics of these 173 patients are noted on Table I.17, including the method of payment. Previous reports indicated that 4% to 16% of patients in long-term care facilities receive systemic antibiotics at any point in time (Garibaldi et al, 1981; Characteristics of nursing home residents, 1981; U.S. Department of Health, 1976; Standfast et al, 1984).

The most common suspected sites of infection were urinary tract (58.4), lower respiratory tract (19.1%) and skin or subcutaneous tissue (4.6%), including infected decubiti or pressure sores, (Table I.18.)

The documentation of the physician's response to and workup for the suspected infections, prior to the antibiotic order, are summarized in Table I.19. Of the 173 total infections, localizing signs or symptoms were recorded in less than half, and appropriate cultures ordered and diagnoses recorded in approximately one-third. For the two most common sites of infections; urinary and lower respiratory tracts, both tests and cultures were ordered in approximately two-thirds and one-quarter, respectively. Previous reports indicated that the pretreatment cultures were obtained in 11% to 35% of antibiotic treated episodes (Howard et al, 1976; Brown and Thompson, 1979).

The evidence for infection at the time of the initial antibiotic order is noted in Table I.20. Localizing signs or symptoms were recorded in the chart in less than half of the cases. A positive culture was available in approximately one-quarter of the 173 total suspected infections and fever was noted in a similar proportion. In patients being treated for suspected urinary tract infection, the commonest site, approximately half had a positive urinalysis and/or culture at the time of the order. Of the 33 lower respiratory infections, approximately one-fifth had a positive chest x-ray or sputum culture.

The systemic antibiotics ordered are listed in Table I.21 for all sites and for the two most frequent ones, urinary tract and lower respiratory tract. Trimethaprim-sulfamethoxazole, a favorite oral broad-spectrum agent, was ordered for nearly 45% of the 173 total infections and accounted for more than one-half of the regimens for urinary tract infections. Ampicillin or amoxicillin was ordered for nearly one-fifth of the infections including over half of the lower respiratory tract infections. Nitrofurantion, sulfonamides and methenamine mandelate accounted for approximately 30% of the regimens for urinary tract infection. With the exception of cefazolin, cephadrine and gentamicin, which were given intramuscularly, all of the treatment regimens employed oral antibiotics.

3. Antibiotic Utilization and Expenditure. For this review we searched the Index Medicus and identified 28 titles that suggested that they might be relevant to this Task. In general, these sources could be divided into four major categories:

1) One set of titles discussed drug expenditures and purchases but did not include references to antibiotics. Some examples of the more recent studies included: Baum et al, 1985a; Simonson, 1984; Reynolds, 1984; Knapp, 1984; Vener et al 1979.

2) A second set of references mentioned antibiotics but failed to include age-specific data. Some examples of the more recent studies included: Baum et al, 1985b; Kennedy et al, 1983; Stevens et al, 1981; Kass, 1978; Schaffner et al, 1978.

3) The third set presented data on utilization and/or

expenditure of drugs by the elderly and included information on antibiotics. Some examples of the more recent studies included: Lamy, 1980; U.S. Department of Health, 1976; and Shapiro et al, 1979.

4) A fourth set of reports was categorized as miscellaneous because, although the information was recorded was pertinent, the title did not suggest this. Some examples of the more recent studies included: Borden & Lee, 1982.

In addition, we reviewed two special reports: U.S. Department of Health, 1979 and U.S. Senate Special Committee on Aging, 1981. Neither had information on antibiotics.

The references since 1979 that provided the most relevant information are summarized here.

Simonson (1984) provided a summary of the demographics regarding financial considerations of health and medication consumption (Table 1.22 [Tables 2-1 to 2-5]). This information may provide helpful background on national statistics but there were no references to drug categories, including antibiotics.

Baum and colleagues (1985a) using data purchased by the FDA from IMS, America Ltd., the National Prescription Audit (NPA) and the National Drug Therapeutic Index (NDTI), provided 1982 national estimates of age differences in out-patient use of major drug categories. From NDTI data the most frequent prescribed drug categories were identified for patients 65 years of age and older (Table I.23). Antibiotics do not appear on this list.

Baum and collaborators (1985b) again provided 1982 national estimates for drug use and expenditure, using similar data sources for out-patients and the U.S. Pharmaceutical Market-Hospitals (USH) data for hospitalized patients. As noted in Table I.24 (Table 1) persons 60 years of age and older represented only 16% of the population but accounted for 30% of all visits to office-based physicians and 38% of the total drug mentions reported to the NDTI. [Table 3] lists 16 major therapeutic classes that accounted for more than 3/4 of the total drug store and hospital expenditures for ethical pharmaceuticals (includes all prescription drugs and those over-the-counter products that are promoted to health professionals). Antibiotics (anti-infectives) alone account for 1/3 of the hospital total but less than 10% of the drug store expenditures. No age- or disease-specific data was reported.

Kennedy and colleagues, (1983) provided the first report on hospital antibiotic use at a national level. Single-entity systemic antibiotics currently marketed in the United States were evaluated from 1981 antibiotic purchases by 450 non-federal short-term general hospitals or psychiatric hospitals from the USH data collections of IMS America, Ltd. Drug use was measured in defined daily doses (DDDs), which represent the average maintenance dose for the primary indication, per 100 bed-days. By dividing annual hospital purchases of each drug by the DDD and the annual number of patient days, the resulting figure provided an estimate of the proportion of hospitalized patients exposed to each drug. Enough single-entity antibiotics were purchased by U.S.

hospitals in 1981 to provide a total of approximately 74 DDDs/ 100 bed-days. Data on individual antibiotics for each DDD and the cost figures for parenteral forms likely to be used in life-threatening infections are presented in Table I.25 [Table 1] and I.25a, respectively. Problems with this method of data analysis include 1) the fact that conservative DDD estimates overestimate actual exposures of patients for drugs that have wide dose ranges and 2) a lack of linkage to patient demographics (age) and clinical data (disease).

Stevens and colleagues (1981) studied 464 patients in a regional tertiary care hospital. One or more antibiotics (excluding topical and non-absorbable oral agents) were administered to 170 (36.6%) of patients (Table I.26 [Table 4]). The individual antibiotics are listed but no age-specific or disease-specific data was provided. [Table 5] compares the sites of infection in the 1971 and 1979 surveys; again no age-specific data is available.

Shapiro and co-investigators (1979) surveyed the hospital charts of 5,288 patients in 20 hospitals that were randomly selected from the 194 general hospitals in Pennsylvania. Systemic antibiotics, oral or parenteral, were administered to 28% of the patients. The proportion of patients receiving antibiotics increased with age ranging from 22% in the pediatric age group to 49% of those 85 years of age or older (Table I.27 [Table 2]). Persons 65+ years of age accounted for 20% of the total patients but nearly 40% of the patients receiving antibiotics. This association of increased age and antibiotic use in the hospital setting is probably related to the increased rates of hospital-acquired infections in older patients (Gross et al, 1963). [Table 5] lists the distribution of antibiotic courses by drug group. There was no correlation provided between age, disease or antibiotic group.

Lamy (1980) cited several reports with pertinent information. Studies of drug use in community-based older persons who receive care in day treatment centers indicated that antibiotics are infrequently ordered on a PRN basis (Table I.28a [6.6]). Studies in nursing homes indicate that the proportion of residents/patients receiving antibiotics ranged from 16.5% to less than 1% table I.28b [6-9 and 6-11]. No details are provided to assess why this variability exists. In the community setting, antibiotics are prescribed for less than 3.5% of elderly patients [Table 6-14]. No information was provided on specific infections or age-specific data on antibiotic use.

Borden and Lee (1982) reported a pharmacy-based prospective study of 21,372 patients, mean age 25 years old, treated with oral antibiotics administered in an ambulatory-care setting. Four antibiotics, erythromycin, penicillin V, ampicillin and tetracycline accounted for 78% of all prescriptions. Table I.29 [7] summarizes the distribution within each age group for the most frequently prescribed antibiotics. In comparison to adults 18-49 years of age, persons 65+ years old received less erythromycin and penicillin prescriptions and more tetracycline (including doxycycline), cephalexin and "other" antibiotics not further described. It is not apparent how serious these infections were. No further information is provided to assess this difference but it probably is due to the decreased rates of upper respiratory tract and mycoplasma infections for which penicillin and erytnromycin are frequently prescribed. Of the o2 hospital admissions in the 30 days following the prescription, nine were for infections but there is no information correlating these cases with the patients receiving antibiotics.

The Long-term Care Facility Improvement Study (U.S. Department of Health, 1976) examined physicians' prescribing patterns in skilled nursing facilites. The nursing home survey data was drawn from a sample of 288 homes representing a total of 6,591 homes and a sample of 3,458 residents, respresenting a total of 288,915 residents, who were being reimbursed through Medicare/Medicaid programs. The 221,029 residents, who were 65+ years of age, represented 78% of all patients. Most homes were served by community pharmacies and, for the most part, verbal (telephone) orders were given by the physician. Of the 1,731,360 prescriptions, 3% were for systemic oral or parenteral antibiotics (anti-infectives) and 16% of the 283,914 total patients were receiving an antibiotic at any one time (Table I.30 [6]). The number and percent of antibiotics, by subclass, is noted in Table I.31 [A-10]. This study included patients receiving prophylactic antibiotics.

In summary, there is little published data on antibiotic utilization in older patients and no information on specific infections except for the unpublished observations of Zimmer and colleagues

(1985) in nursing homes. In general, older patients receive more antibiotics in hospital > nursing home > community. This is due to the relative rates of bacterial infection in each of these settings and the opportunities for documentation.

B. Data From Special Information Services. As noted in the literature review, detailed information on antibiotic utilization and expenditure for the four specific infections in hospitals, nursing homes and the community is incomplete, especially for national figures. To provide additional information several special information services or data systems were contacted. Table I.32 a-e lists these services, the data available for the report and any special comments or problems. To obtain this information the following steps are required:

1) Determine the number and frequency of discharges or encounters of or with residents/patients with each of the four specific diseases. To accomplish this we have provided the services with several pages copied from the International Classification of Diseases, 9th Review, Clinical Modification (Table I.33) or the ICD 7 four-digit diagnosis codes used by IMS (See materials sent to H. Shaman).

2) By cross-tabulation determine the number and frequency of prescriptions by antibiotic subcategory for each of the diagnoses.

3) By cross-tabulation determine the number and frequency of prescriptions for the total population under 50 years of age and for elderly patients age 65-79 and 80+ years old or by decades (65-74, 75-84 and 85+ years of age if the elderly population is

large enough).

4) Estimate the expenditures to treat elderly patients with these specific diseases by determining the mean daily dose and duration of treatment.

Preliminary discussions with these services suggests that the information is available and that it is possible to link specific disease with prescription and age of patient. Several services, however, can only provide information on what is already available; any new work requires additional programming which entails a substantial cost.

With the exception of information from IMS America, Ltd., and a letter of intent from Health Information Designs, it is unlikely that the antibiotic contract will be able to provide the information requested on Antibiotic Utilization and Expenditure. All letters of agreement (or refusal) from the special information services contacted were enclosed in a separate mailing to H. Shaman. It is recommended that OTA contact these services for any further work in this area.

C. Transfers from Nursing Homes to Hospitals.

Hospitalization of nursing home patients is a common, costly and potentially preventable occurrence. According to the most recent National Nursing Home Survey (1977), there were some 340,000 hospitalizations from 1,402,200 nursing home beds in the U.S., an annual rate of about 250 per 1000 beds. The role of infection (specifically pulmonary, urinary tract, skin infections) and the use of antibiotics in these hospitalizations is the subject of the following literature review and the data analysis contained in Appendix H. The following aspects of this issue are addressed:

1. Frequency of transfer to hospital for treatment of fever or infection. This includes comparison with frequency of such hospitalizations of community dwelling elderly.

2. Frequency of transfer for the three specific infections under consideration.

3. Estimate of antibiotic utilization for such hospitalizations.

4. Assessment of factors influencing the decision to hospitalize and to specifically treat serious infections when they occur in nursing homes.

Literature Review

While the transfer of patients from hospital to nursing home has received extensive attention in the past decade, the transfer of nursing home residents to acute hospital has only recently begun to receive attention. A number of such studies have been published or presented at national meetings in the past several years (Irvine 1984, Tresch 1985, Mott 1985, Gabow 1985, Brown 1979, Van Buren 1982, Stark 1982, Gillick 1983, Goldstein 1984, Gordon 1985, Lewis 1985, Shapiro 1985). Among these studies the first seven specifically address the role of fever or infection. These are listed on the accompanying table, which includes for each study the geographic setting, elements of study design and summary of findings with respect to infection. It will be noted that information on the specific infections of interest is provided in five of the seven studies.

1. Frequency of transfer for treatment of infection or fever.

- Fever or infection was the primary reason or a major co-morbidity in approximately 30% of hospitalizations of nursing home residents, among this series of studies. The three studies (A,F,G) which collected comparable data on hospitalization of community-dwelling elderly noted that fever/infection accounted for much smaller proportions of these hospitalizations (2%, 3%, and 12% respectively).

2. Frequency of hospitalization for specific infections

Proportion of all hospitalizations

Pneumonia accounted for 6% of all hospitalizations in study B, 12% in study A, 15% in study D, and 31% in study C. Urinary tract infection, usually with sepsis, accounted for 8% of all hospitalizations in study A, 10% in study B and 20% in study C. Skin/decubitus ulcer infection accounted for 3% of hospitalizations in study A, but were not mentioned in the data on hospitalization in the other studies.

Proportion of infection hospitalizations

Among all hospitalizations for infection, pneumonia and urinary tract infection accounted for the majority of instances, while skin/decubitus ulcer infection was seen infrequently. These data, available from three studies are shown in the following table:

Hospitalizations Caused by Infection

Number (% of Total)

Study	Pneumonia	UTI	Skin/Decubitus	Other	Total
Irvine, et al (2)	15(44)	10(30)	4(11)	5(15)	34(100)
Tresch, et al (3)	4(22)	6(33)	--	8(44)	18(100)
Mott, Barker (4)	40(55)	26(36)	--	7(9)	73(100)

3. Antibiotic Utilization

Specific details regarding types and amounts of antibiotics utilized in treating nursing home patients hospitalized for infection are not provided in any of the studies. One study notes that oral or intra-muscular antibiotic had been initiated in the nursing home prior to hospital transfer in 11 of 18 (61%) admissions for infection (Tresch, et al 1985). All 18 of these patients were treated with intravenous antibiotics once hospitalized; infeact the need to administer antibiotics intravenously was mentioned as a principle reason for most of these transfers occurring. On the assumption that specific treatment with antibiotics was administered in essentially all hospitalizations for infection, it is possible to estimate antibiotic utilization per hospitalization from data on usual amount antibiotics per day for the specific infections and estimates of the average number of days of treatment. (Data for making these estimates for the four specific infections are found in Task I, section VII. A.1.b. and tables I.13-I.15 of this report).

4. Determinants of transfer to hospital for infection

The decision whether or not to transfer a nursing home patient with an acute and potentially life-threatening infection to an acute care hospital, and hence to receive full antibiotic treatment, may be influenced by several distinctive factors, as discerned from this review.

First is the existence of a system whereby prior directives are routinely solicited from the patient, when and if mentally competent, or by family members of an incompetent patient, and have been made known to the attending medical and nursing staff. Such prior directives are extensively discussed in Task 2 of this report: Among the studies reviewed, the role of prior directives was clearly evident in the experience reported by Mott and Barker (See appendix H of this report) in which disproportionately smaller numbers of pneumonias and UTI's among patients in the "comfort care only" category were hospitalized.

Secondly, it is apparent in the study by Brown and Thompson (1979), that even in the absence of a routine system for soliciting patient prior directives, heroic treatment with antibiotics and hospitalization was witheld from a substantial number of nursing home patients. Factors significantly associated with such decisions included medical diagnoses with clearly poor prognosis (particularly cancer), and/or advanced degree of mental or physical incapacity.

A third element noted also by Brown and Thompson is the relation of physician to the patient. Consultatnt or alternate physicians unfamiliar with patients were more likely to treat infections than were physicians who were regularly in touch with the patient. Pertinent to this issue, the role of continuity of medical care in influencing treatment decisions, are several other observations. In a review of hospitalizations of nursing home patients for all causes, including infection, physician visiting at time of acute illness was associated with avoidance of hospitalization (Van Buren et al, 1982). In a project in Boston in which physician-nurse practitioner teams provide care for a large panel of nursing home patients, including regular visits to evaluate and treat episodes of acute illness, the rate of hospital utilization for acute illness has been significantly less than for comparable groups of patients without such continuity of medical care (Master et al, 1980).

Finally, a strictly medical reason for hospitalizing nursing home patients with acute infection is the need to administer intravenous antibiotics. This was the primary reason for transferring both pneumonias and UTIs with sepsis in the study by Tresch et al, 1985. While not mentioned in other studies, this is probably an important factor in many transfers of patients with acute infections to hospital, because in most instances nursing homes are not adequately staffed or equipped to properly administer intravenous antibiotics. By contrast, as discussed elsewhere in this report under "international experiences," acute infections are rarely transferred to acute hospitals from longstay institutions in Great Britian because these medically-monitored units are able to administer intravenous antibiotics as needed.

Task I.
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Figure I.1

THE DECISION-MAKING PROCESS FOR ANTIBIOTIC TREATMENT

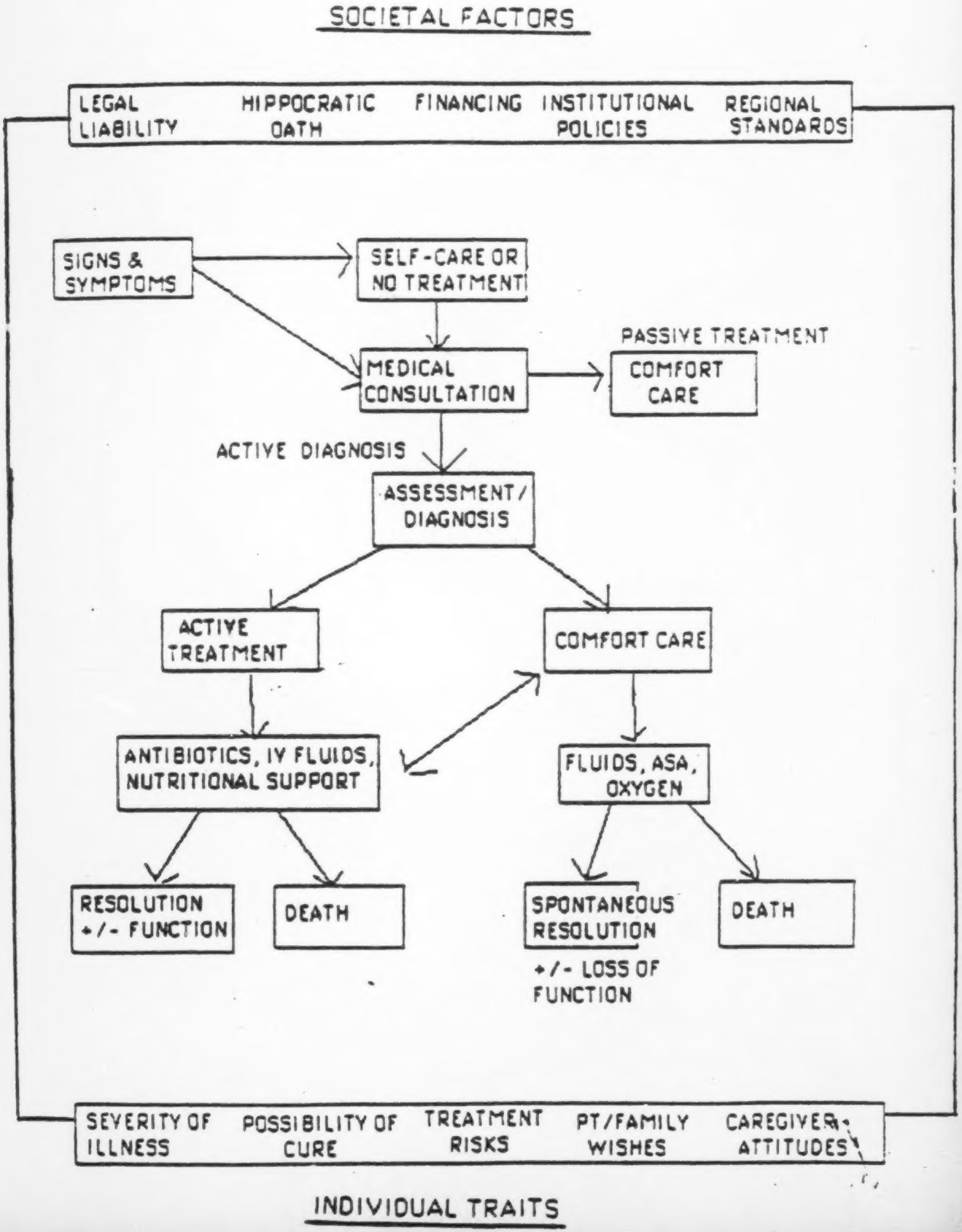


Table I.2 Major Types of Device-Related Infections

Device	Hospitalized Patients with Device	Related Infections	Those with Device Developing Infection	Estimated Number of Cases Annually* (Patients 65+)[a]	Case-Fatality Ratio
	%		%		%
Infections related to commonly used devices					
Urinary catheter	10	Bacteriuria	20	760 000 (186,200)	<1
		Epididymitis	...	...	...
		Septicemia	0.5 to 2.5	28 500 (698)	20 to 40
Intravascular infusion†					
Scalp vein needle	12	Suppurative phlebitis	<0.01		
		Septicemia	<0.1	... 2280 (559)	20 to 40
Plastic catheter	12	Suppurative phlebitis	...	...	
		Septicemia	0 to 8	22 800 (5586)	20 to 40
Subclavian catheter	0.5	Suppurative phlebitis	...	...	
		Septicemia	3 to 7	7600 (1862)	20 to 40
Total parenteral nutrition	0.1	Suppurative phlebitis	...	...	
		Septicemia	0 to 27	2700 (661)	20 to 40
Arterial catheter	0.2	Arteritis (?)	...	...	
		Septicemia	0.2	150 (37)	20 to 40
Respiratory therapy					
Continuous ventilator	2	Tracheitis	...	...	5
		Pneumonia	...	51 650 (12,654)	40
Intermittent positive-pressure breathing	7	Pneumonia	...	12 120 (2969)	40
Infections related to specialized devices					
Hemodialysis	...	Hepatitis	3 to 35	...	5 to 10
		Septicemia	20 to 25	...	10 to 20
		Shunt infection	15 to 20	...	<5
Cerebrospinal fluid shunt	...	Ventriculitis	6 to 23	...	30 to 35
		Septicemia	Variable	...	30 to 35
Prosthetic heart valve	...	Endocarditis	1 to 2	...	50 to 60
Vascular graft	...	Graft infection	1.3 to 1.5	...	20 to 45
Artificial hip	...	Deep wound	0 to 10	...	5 to 45
Prosthetic lens	...	Endophthalmitis	...	...	...

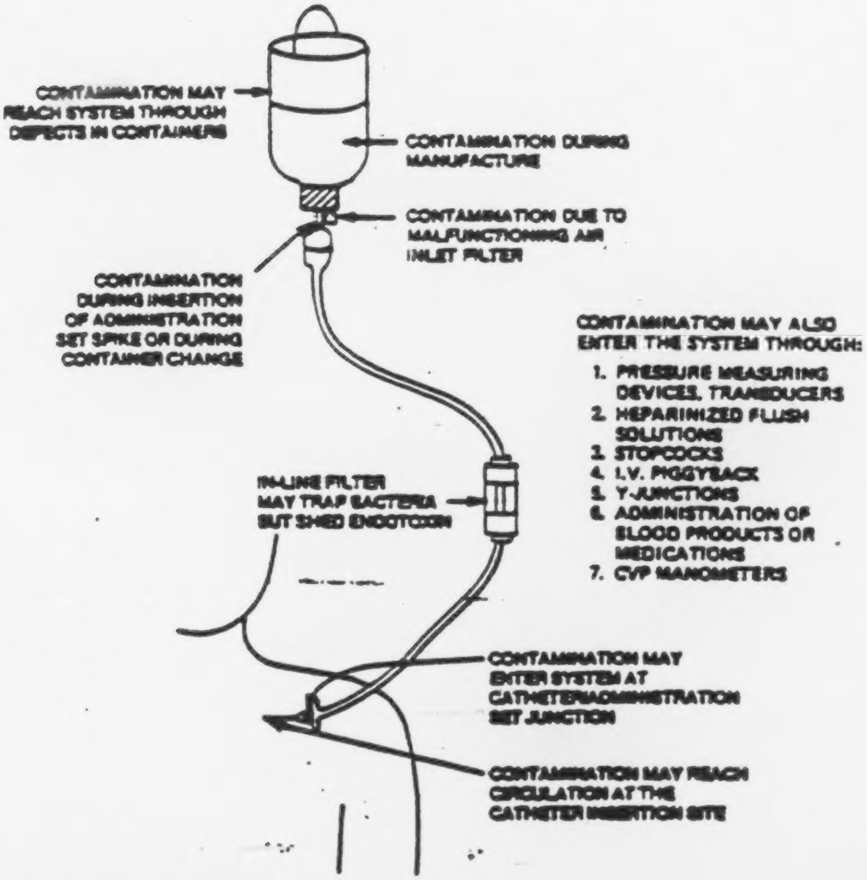
* Calculations based on 38 million acute-care hospital admissions annually times percent of hospitalized patients with each device times estimated rate of device-associated infection. With pneumonia, rates of device-associated infections are unavailable, and estimates were derived as described in the text. Since use of the specialized devices noted above varies widely from hospital to hospital, neither the percent of hospitalized patients with these devices nor the number of infections occurring annually could be accurately estimated.

† Catheter phlebitis was not included among device-related infections (see text).

[a] Estimate for patients 65+ based on 9.3 million medicare-reimbursed admissions to acute care hospitals in 1980 (or 24.5% of 38M) and assumes there is a proportionate rate of device-associated infections in these patients-both assumptions probably underestimate the actual rates in elderly patients.

(Modified from Stamm, WE. Infections Related to Medical Devices. Ann Int Med 1978;89:764-769)

Figure I.3 Points of Access for Microbial Contamination in Infusion Therapy


CONTAMINATION MAY REACH SYSTEM THROUGH DEFECTS IN CONTAINERS
CONTAMINATION DURING MANUFACTURE
CONTAMINATION DUE TO MALFUNCTIONING AIR INLET FILTER
CONTAMINATION DURING INSERTION OF ADMINISTRATION SET SPIKE OR DURING CONTAINER CHANGE
CONTAMINATION MAY ALSO ENTER THE SYSTEM THROUGH:
1. PRESSURE MEASURING DEVICES, TRANSDUCERS
2. HEPARINIZED FLUSH SOLUTIONS
3. STOPCOCKS
4. I.V. PIGGYBACK
5. Y-JUNCTIONS
6. ADMINISTRATION OF BLOOD PRODUCTS OR MEDICATIONS
7. CVP MANOMETERS
IN-LINE FILTER MAY TRAP BACTERIA BUT SHED ENDOTOXIN
CONTAMINATION MAY ENTER SYSTEM AT CATHETER/ADMINISTRATION SET JUNCTION
CONTAMINATION MAY REACH CIRCULATION AT THE CATHETER INSERTION SITE

(Data from Henderson DK. Bacteremia Due to Percutaneous Intravascular Devices. In: Mandell GA, Douglas RG Jr, Bennett JE, eds. Principles and Practice of Infectious Diseases. New York:1985:1612-20)

Table I.4 Patient-Related Risk Factors For Device-Associated Bacteremia

---

Age ≤ 1 year, ≥ 60 years

Granulocytopenia

Immunosuppressive chemotherapy

Loss of skin integrity (e.g., burns, psoriasis)

Severity of underlying illness

Presence of distant infection

(Data from Henderson DK. Bacteremia Due to Percutaneous Intravascular Devices. In: Mandell GA, Douglas RG Jr, Bennett JE, eds. Principles and Practice of Infectious Diseases. New York: 1985:1612-20)

Table I. 5 Total Parenteral Nutrition-Related Infections: Comparison of Risk Factors Among Courses With and Without Infection.

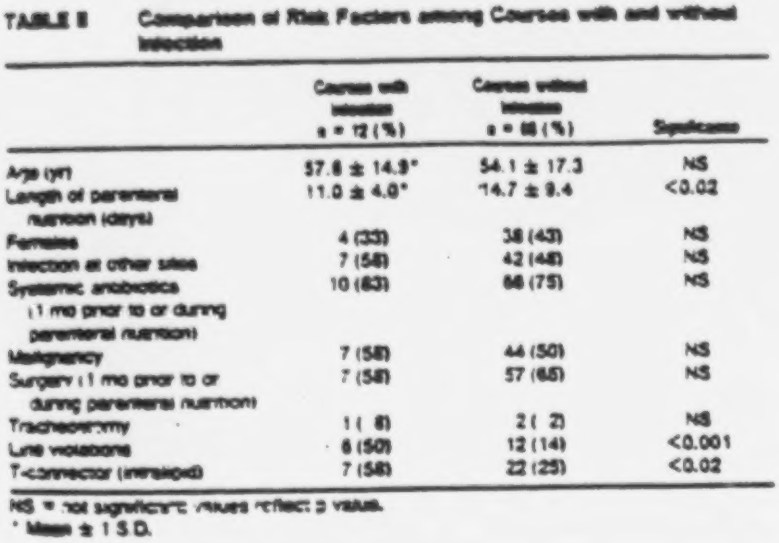


TABLE II Comparison of Risk Factors among Courses with and without Infection

	Courses with infection n = 12 (%)	Courses without infection n = 88 (%)	Significance
Age (yr)	57.8 ± 14.9*	54.1 ± 17.3	NS
Length of parenteral nutrition (days)	11.0 ± 4.0*	14.7 ± 9.4	<0.02
Females	4 (33)	38 (43)	NS
Infection at other sites	7 (58)	42 (48)	NS
Systemic antibiotics (1 mo prior to or during parenteral nutrition)	10 (83)	66 (75)	NS
Malignancy	7 (58)	44 (50)	NS
Surgery (1 mo prior to or during parenteral nutrition)	7 (58)	57 (65)	NS
Tracheostomy	1 (8)	2 (2)	NS
Line violations	6 (50)	12 (14)	<0.001
T-connector (intralipid)	7 (58)	22 (25)	<0.02

NS = not significant; values reflect p values.

* Mean ± 1 S.D.

(Data from Snydman DR et al. Total Parenteral Nutrition-Related Infections: Prospective Epidemiologic Study Using Semiquantitative Methods. Am J Med 1982;73:695-699)

Table I.6 Estimated Prevalence of Eitologic Agents Causing Bacterial Pneumonia in the Elderly According to Setting

	COMMUNITY-ACQUIRED	INSTITUTION-ACQUIRED	HOSPITAL ACQUIRED
S. pneumonia	55%	35%	20%
H. influenzae and Hemoophilus species	10%	5%	5%
S. aureus	1%	1%	5%
Gram. neg. bacilli	5%	15%	35%
Mixed flora [a]	25%	40%	30%
Other [b]	4%	4%	5%

[a] Two or more respiratory pathogens, normal oropharngeal commensals or both

[b] Other = L. pneumophilia, anaerobes, fungi, unknown

(Data from Bentley DW, Mamot K et al: Pneumococcal vaccine in the institutionalized elderly: Design of a nonrandomized trial and preliminary results. Rev Infect Dis 1981; 3s71. Ebright JR, Rytel MW. Bacterial pneumonia in the elderly. J Am Geriatr Soc 28:220. 1978: and Verghese A, Berk SL. Bacterial pneumonia in the elderly. Medicine 62:271, 1983)

Table I·7 Estimated Prevalence of Etiologic Agents Causing UTIs in the Elderly According to the Setting

	COMMUNITY-ACQUIRED	INSTITUTION-ACQUIRED	HOSPITAL-ACQUIRED
E. coli	21-72%[a]	20-38%	34%
Klebsiella sp.	24-5%	6-28%	10%
Proteus sp.	12-17%	29-18%	11%
Ps. aeruginosa	7-0%	13-8%	31%
Other gram-bacilli	4-3%	12-8%	0%
Enterococci	9-3%	10-0%	14%
Other gram + organisms	23-0%	8-0%	0%
Polymicrobial	30-10%	30%-30%	NI

[a] Hypnenated percentages indicate prevalence for men-women.

NI, no information.

(Data from Aktar AJ, Andrews GR, Caird FL et al: Urinary tract infection in the elderly female: Urinary tract infection. Proceedings of the 2nd National Symposium, March 1972, Oxford, Oxford University Press, 1973: Sherman FT, Tucci V, Libow LS et al: Nosocomial urinary tract infections in a skilled nursing facility. J Am Geriatr Soc 28:456. 1980: and Wolfson SA, Kalmanson GM, Rubini ME et al: Epidemiology of bacteruria in a predominantly geriatric male population. Am J Med Sci 250:168, 1965)

Table I.8 Microbiology of Infected Pressure Sores in 21 Patients, Including 16 with Bacteremia

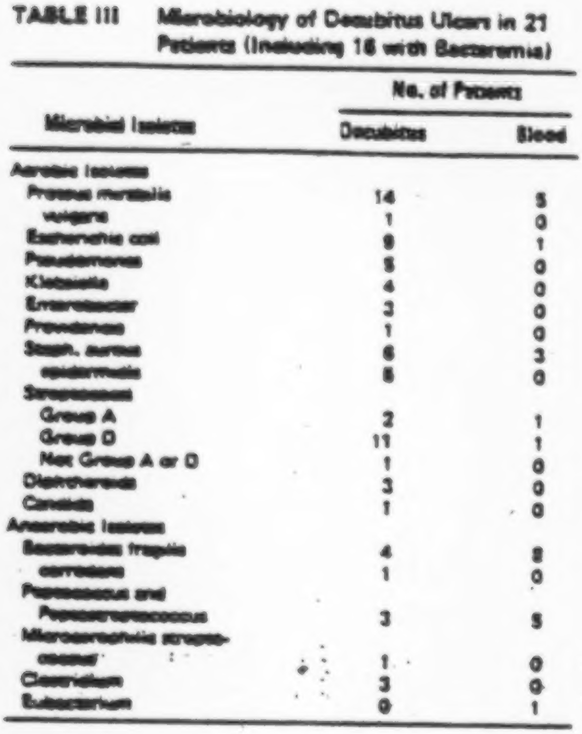
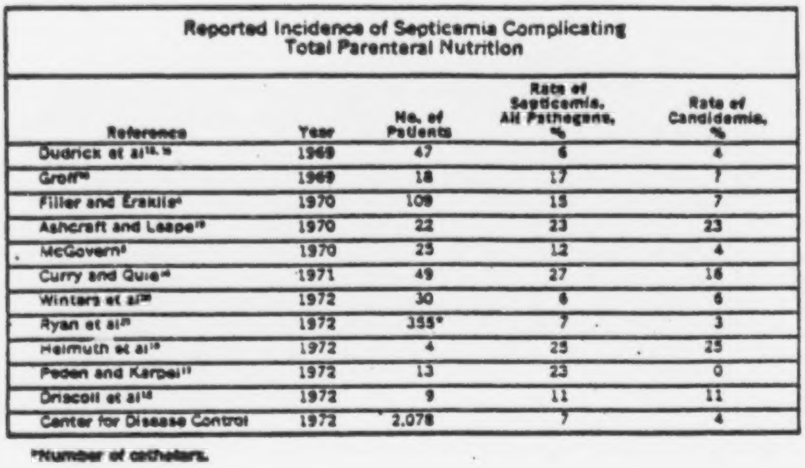


TABLE III Microbiology of Decubitus Ulcers in 21 Patients (Including 16 with Bacteremia)

Microbial Isolates	No. of Patients	
	Decubitus	Blood
Aerobic isolates		
Proteus mirabilis	14	5
vulgaris	1	0
Escherichia coli	9	1
Pseudomonas	5	0
Klebsiella	4	0
Enterobacter	3	0
Providencia	1	0
Staph. aureus	6	3
epidermidis	8	0
Streptococci		
Group A	2	1
Group D	11	1
Not Group A or D	1	0
Diphtheroids	3	0
Candida	1	0
Anaerobic isolates		
Bacteroides fragilis	4	8
corrodens	1	0
Peptococcus and Peptostreptococcus	3	5
Microaerophilic streptococcus	1	0
Clostridium	3	0
Eubacterium	0	1

(Data from Galpin JE, Chow, AW, Bayer AS, Guze LB. Sepsis Associated with Decubitus Ulcers. Am J Med 1976; 61:346-350)

Table I. 9 Reported Incidence of Septicemia
Complicating Total Parenteral Nutrition
In Hospitalized Patients



Reported Incidence of Septicemia Complicating Total Parenteral Nutrition

Reference	Year	No. of Patients	Rate of Septicemia, All Pathogens, %	Rate of Candidemia, %
Dudrick et al[15,16]	1969	47	6	4
Groff[20]	1969	18	17	7
Filler and Eraklis[4]	1970	109	15	7
Ashcraft and Leape[19]	1970	22	23	23
McGovern[8]	1970	25	12	4
Curry and Quie[4]	1971	49	27	16
Winters et al[20]	1972	30	6	6
Ryan et al[21]	1972	355*	7	3
Helmuth et al[10]	1972	4	25	25
Peden and Karpel[11]	1972	13	23	0
Driscoll et al[13]	1972	9	11	11
Center for Disease Control	1972	2,078	7	4

*Number of catheters.

(Data from Goldmann DA, Maki DG. Infection Control in Total Parenteral Nutrition. JAMA 1973;223:1360-1364)

Table I. 10 Age Distribution of Survey Population and Patients with Pressure Sores

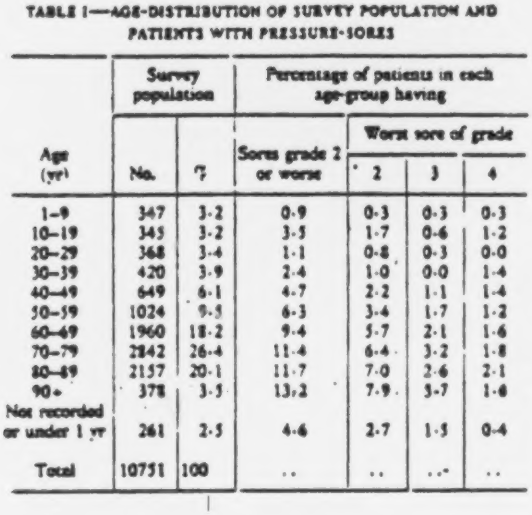


TABLE I—AGE-DISTRIBUTION OF SURVEY POPULATION AND PATIENTS WITH PRESSURE-SORES

Age (yr)	Survey population		Percentage of patients in each age-group having			
				Worst sore of grade		
	No.	%	Sores grade 2 or worse	2	3	4
1–9	347	3·2	0·9	0·3	0·3	0·3
10–19	345	3·2	3·5	1·7	0·6	1·2
20–29	368	3·4	1·1	0·8	0·3	0·0
30–39	420	3·9	2·4	1·0	0·0	1·4
40–49	649	6·1	4·7	2·2	1·1	1·4
50–59	1024	9·5	6·3	3·4	1·7	1·2
60–69	1960	18·2	9·4	5·7	2·1	1·6
70–79	2842	26·4	11·4	6·4	3·2	1·8
80–89	2157	20·1	11·7	7·0	2·6	2·1
90+	378	3·5	13·2	7·9	3·7	1·6
Not recorded or under 1 yr	261	2·5	4·6	2·7	1·5	0·4
Total	10751	100	..	..	..	..

(Data from Barbenel JC, Jordan MM, Nicol SM. Incidence of Pressure-Sores in the Greater Glasgow Health Board Area. Lancet 1977; ii:548-550)

Table I.11 Estimated Prevalence of Bacteriuria According to Age and Level of Care

AGE	WOMEN	MEN
<65 Home	5%	<1%
65-79	20%	10%
80+	40%	20%
65+ Nursing Home	25%	20%
65+ Acute Hospital	30%	30%
65+ Chronic Disease Hospital	40%	35%

(Modified from Kaye D:Urinary Tract infections in the elderly. Bull NY Acad Med 56:209,1980)

Visits with p[redacted] as first-, second-, or third-listed diagnosis, by patients age and type of antimicrobial drug ordered or provided: US, 1980 and 1981

NATIONAL AMBULATORY MEDICAL CARE SURVEY-NCHS
1980-81 VISITS -ANTIBIOTIC GROUP TAPE

TABLE 1

PLANE 1
PART 1- 1

PAGE 1
27 AUG 1983

= ALL

Table I.12 ⓐ Community Estimates for Bacterial Pneumonia

ROWS = MAJOR SYSTEMIC GROUPS ONLY   COLUMNS = AGE GROUPS FOR REQUEST

	ALL	UNDER 50	50-64	65-79	80 AND OVER	KEY
ALL	323	191	74	43	15	RAW ← Number of sample records on which national estimate is based.
	4759343	2981993	1076842	543904	157404	WTI ← Weighted national estimate (unrounded)
	100.000	100.000	100.000	100.000	100.000	WIC ← Column percentage
	100.00	62.66	22.61	11.43	3.31	WIR ← Row percentage
SYSTEMIC	199	138	37	18	6	RAW
ANTIBIC	3025972	2157236	541097	247017	80622	WTI
VISITS	63.580	72.342	50.206	45.416	51.220	WIC
	100.00	71.29	17.88	8.16	2.66	WIR
PENI-	96	67	20	6	3	RAW
CILLINS	1292640	979564	178097	85094	49805	WTI
	27.160	32.849	16.551	15.645	31.692	WIC
	100.00	75.78	13.78	6.58	3.86	WIR
CEPHALO-	23	18	3	2		RAW
SPORINS	315791	272775	31112	11904		WTI
	6.635	9.147	2.891	2.189		WIC
	100.00	86.38	9.85	3.77		WIR
MACRLIDS	68	43	9	6	2	RAW
AND LIN-	1254569	847732	272272	108658	25907	WTI
COSAMDES	26.360	28.428	25.303	19.977	16.459	WIC
	100.00	67.57	21.70	8.66	2.07	WIR
TETRA-	18	9	5	3	1	RAW
CYCLINES	210104	113764	56474	35036	4830	WTI
	4.415	3.815	5.248	6.442	3.069	WIC
	100.00	54.15	26.88	16.68	2.30	WIR
SULFONDS	7	4	1	2		RAW
AND OR	75693	53877	10132	11684		WTI
TRIMETHP	1.590	1.807	0.942	2.148		WIC
	100.00	71.18	13.39	15.44		WIR
OTHER	3	3				RAW
ANTIBTICS	49812	49812				WTI
	1.047	1.670				WIC
	100.00	100.00				WIR
Non-antimicrobial [illegible]	1,733,371	824,757	534,945	296,887	76,782	

NOTE:
1) Visit estimates ≤ 448,000 do not meet NCHS standards of statistical reliability.
2) Columns may be added (i.e., age groups may be combined) because each patient had only one age, but rows may not be added (i.e., drug types may not be combined) because some patients were ordered or provided with more than one type of drug.

Visits with ~~[illegible]~~ the first-, second-, or third-listed diagnosis, by patients age and type of antimicrobial drug used: US, 1980 and 1981

NATIONAL AMBULATORY MEDICAL CARE SURVEY-NCHS
1980-81 VISITS -ANTIBIOTIC GROUP TAPE

= ALL

Table I.17D Community Estimates for Urinary Tract Infections

ROWS = MAJOR SYSTEMIC GROUPS ONLY   COLUMNS = AGE GROUPS FOR REQUEST

See NOTES on pneumonia table

	ALL	UNDER 50	50-64	65-79	80 AND OVER	KEY
ALL	1217	706	242	215	54	RAW
	16003063	8922115	3390584	2990860	699576	WTI
	100.000	100.000	100.000	100.000	100.000	WIC
	100.00	55.75	21.19	18.69	4.37	WIR
SYSTEMIC ANTIMIC OBJETS	838	501	152	148	37	RAW
	11281621	6364642	2409941	2032550	474488	WTI
	70.497	71.336	71.079	67.959	67.825	WIC
	100.00	56.42	21.36	18.02	4.21	WIR
PENI-CILLINS	129	89	21	16	3	RAW
	1832196	1248857	341085	214573	27681	WTI
	11.449	13.997	10.060	7.174	3.957	WIC
	100.00	68.16	18.62	11.71	1.51	WIR
CEPHALO-SPORINS	75	54	12	5	4	RAW
	991662	665725	194930	51991	79016	WTI
	6.197	7.462	5.749	1.738	11.295	WIC
	100.00	67.13	19.66	5.24	7.97	WIR
MACROLIDS AND LIN-COSAMIDES	12	8	3	1		RAW
	287812	116441	167483	3888		WTI
	1.798	1.305	4.940	0.130		WIC
	100.00	40.46	58.19	1.35		WIR
TETRA-CYCLINES	100	71	18	9	2	RAW
	1333281	876991	273425	136380	46485	WTI
	8.331	9.829	8.064	4.560	6.645	WIC
	100.00	65.78	20.51	10.23	3.49	WIR
SULFONDS AND OR TRIMETHP	390	227	68	75	20	RAW
	5367786	2867388	1090103	1155458	254757	WTI
	33.542	32.138	32.152	38.633	36.416	WIC
	100.00	53.42	20.31	21.53	4.75	WIR
OTHER ANTIMICS	157	75	35	37	10	RAW
	2027446	919152	467602	527650	113034	WTI
	12.669	10.302	13.792	17.642	16.158	WIC
	100.00	45.34	23.06	26.03	5.58	WIR

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Visits with [redacted]) as the first-, second-, or third-listed diagnosis, by patients age and type of antimicrobial drug used: US, 1980 and 1981.

TABLE 1
PLANE 1
PART 1- 1
PAGE 1
27 AUG 1985

NATIONAL AMBULATORY MEDICAL CARE SURVEY-NCHS
1980-81 VISITS -ANTIBIOTIC GROUP TAPE

= ALL

Table I.12 Ⓒ Community Estimates for Decubitus Ulcers

ROWS = MAJOR SYSTEMIC GROUPS ONLY

COLUMNS = AGE GROUPS FOR REQUEST

	ALL	UNDER 50	50-64	65-79	80 AND OVER	KEY
ALL	192	59	58	61	14	RAW
	2479117	750740	837720	768724	121933	WT1
	100.000	100.000	100.000	100.000	100.000	WIC
	100.00	30.28	33.79	31.01	4.92	WIR
SYSTEMIC ANTIMIC VISITS	30	9	9	11	1	RAW
	402924	138226	123248	129407	12043	WT1
	16.253	18.412	14.712	16.834	9.877	WIC
	100.00	34.31	30.59	32.12	2.99	WIR
PENI-CILLINS	7	3	1	3		RAW
	83954	52744	7630	23580		WT1
	3.386	7.026	0.911	3.067		WIC
	100.00	62.82	9.09	28.09		WIR
CEPHALO-SPORINS	8	1	5	1	1	RAW
	134971	24701	90497	7730	12043	WT1
	5.444	3.290	10.803	1.006	9.877	WIC
	100.00	18.30	67.05	5.73	8.92	WIR
MACROLIDS AND LIN-COSAMIDES	3	2		1		RAW
	33014	22025		10989		WT1
	1.332	2.934		1.430		WIC
	100.00	66.71		33.29		WIR
TETRA-CYCLINES	2		1	1		RAW
	15760		8791	6969		WT1
	0.636		1.049	0.907		WIC
	100.00		55.78	44.22		WIR
SULFONMDS AND OR TRIMETHP	2	1		1		RAW
	38545	3634		34911		WT1
	1.555	0.484		4.541		WIC
	100.00	9.43		90.57		WIR
OTHER ANTIBICS	9	2	2	5		RAW
	101328	35122	16330	49876		WT1
	4.087	4.678	1.949	6.488		WIC
	100.00	34.66	16.12	49.22		WIR
Non-antimicrobial	2,076,193	620,514	714,472	639,317	109,890	

See NOTES on previous table.

No visit in the 1980 and 1981 sample had V56.0 as one diagnostic code and 038.1, 038.2, 038.3, 038.40, 038.42, 038.43, 038.44, 038.49, or 038.9 as another diagnostic code.

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Table I .13. Recommended Empiric Antibiotic Regimens for Elderly Patients with Life-Threatening Bacterial Pneumonias

Setting	Usual Pathogen(s)	Antibiotics[1]	Maximum Daily Dose (g)[2]	Cost per Day ($)[3]	Minimum Duration (Days)[4]	Cost per Course ($)
Community	Streptococcus pneumoniae mixed flora Hemophilus influenzae gram-negative bacilli	[3rd-generation cephalosporin[5]]	See footnote	[$50.70-168.12]	7	$354.90-1176.84
		or		or		or
		[chloramphenicol]	4.0	[$14.76]		$103.32
		plus		plus		plus
		aminoglycoside[6]	See footnote	$13.40-57.06		$187.60-399.42
Institution						
	Mixed flora Streptococcus pneumoniae gram-negative bacilli	Antipseudomonal penicillins[7] or	See footnote	$76.57-138.40	14	$1072-1937.60
				or		or
		[3rd-generation cephalosporin] or	See footnote	[$50.70-168.12]		$709.80-2353.68
						or
		trimethoprim (TMP) sulfamethoxazole (SMX)[8]	TMP 1.2 SMX 6.0	or [$9.10]		$127.40
		plus		plus		plus
		aminoglycoside	See footnote	$13.40-57.06		$315-798.84
Hospital						
Not Immuno-compromised						
	gram-negative bacilli Staphylococcus aureus Streptococcus pneumoniae mixed flora	[3rd-generation cephalosporin]	See footnote	[$57.70-168.12]	14	$709.80-2353.68
		plus		plus		plus
		aminoglycoside	See footnote	$13.40-57.06		$315-798.84
Immuno-compromised						
	As above plus Legionella pneumophilia	[3rd-generation cephalosporin]	See footnote	[$57.70-168.12]	14	$709.80-2353.68
		plus		plus		plus
		aminoglycoside	See footnote	$13.40-57.06		$315-798.84
		plus		plus		plus
		[erythromycin]	4.0	[$39.16]		$548.24
		plus		plus		plus
		[TMP-SMX]	TMP 1.2 SMX 6.0	[$9.10]		$127.40

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Table I.13. Recommended Empiric Antibiotic Regimens for Elderly Patients With Life-Threatening Bacterial Pneumonia (Continued)

[1] The antibiotic regimen(s) listed first are the drug(s) of choice. The first antibiotic regimen listed within the brackets [] is an alternate choice for penicillin-allergic patients with a history of a delayed hypersensitivity-type reaction. The second antibiotic regimen listed within the brackets is an alternate choice for patients with a history of anaphylactic reaction or interstitial nephritis from either penicillin or cephalosporin. (Data from Bentley DW. Bacterial pneumonia in the elderly: Clinical features, diagnosis, etiology and treatment. Gerontology 1984; 30:297 and Rozas CJ, Goldman AL. Responses to bacterial pneumonia. Geriatrics 1982; 37:61

[2] The recommended maximum daily dose is from Norris, SM and Mandell, GL. Tables of antimicrobial agent pharmacology In: Mandell, GL, Douglas RG Jr and Bennett, JE eds. Principles and Practices of Infectious Diseases, New York, John Wiley and Sons 1985: 308.

[3] The cost per day ($) is from Strong Memorial Hospital Pharmacy, Rochester, N.Y. Total cost to patient is purchase cost + 5% (inventory carrying cost) + $2.40 (dispensing fee) and is noted in the footnotes along with the maximum daily dose for each drug listed.

[4] The recommended minimum duration (days) is an "average" duration for the empirically selected parenteral antibiotics only; it is from Bentley DW. Infectious Diseases. In: I. Rossman (Ed). Clinical Geriatrics. Philadelphia, 1986. In press. J.B. Lippincott. See text for further discussion.

[5] Third-generation cephalosporins (maximum daily dose and cost per day) include cefotaxime (12g; $127.44), cefoperazone (12g; $134.10), moxalactam (12g; $168.12), ceftizoxime (12g; $134.22), ceftazidime (6g; $78.80) and ceftraxone (2g; $50.70).

[6] Aminoglycosides (maximum daily dose and cost per day) include amikacin (1.5g; $57.06), gentamicin (5mg/kg; $13.40), netilmicin (6.5 mg/kg; $24.02) and tobramycin (5 mg/kg; $32.01) [All based on 60kg. patient].

[7] Antipseudomonal penicillins (maximum daily dose and cost per day) include carbenicillin (40g; $76.57), ticarcillin (24-30g; $87.92), pipracillin (24g; $108.24), mezlocillin (24g; $77.16), and azlocillin (24g; $138.40).

[8] Not currently approved for Food and Drug Administration for this indication.

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Table 1.14. Recommended Empiric Antibiotic Regimens for Elderly Patients with Life-Threatening Urinary Tract Infections

Setting	Usual Pathogen(s)	Antibiotics*	Maximum Daily Dose (g)^2	Cost per Day ($)^3	Minimum Duration (Days)^4	Cost per Course ($)
Community	*Escherichia coli*	Ampicillin or	12.0	$22.84 or	14	$319.76
Institution	*Klebsiella sp.*	[Vancomycin]	2.0	[$83.10]		or
or	*Proteus sp.*	plus		plus		$1163.40
Hospital	*Pseudomonas aeruginosa*	aminoglycoside	See footnote	$13.40-57.06		plus
	Enterococcus	or		or		$315.00-798.40
	Polymicrobial	Antipseudomonas	See footnote	$76.57-138.40		or
		penicillins or		or		$1072-1937.60
		[3rd-generation		$50.70-168.12		or
		cephalosporins]				$709.80-2353.68

*See footnotes on Table 1.13 for explanation of brackets [], and individual drugs (plus maximum daily dose and cost per day) in the antibiotic subcategories.

(Data from Gleckman R, Blagg N, Hibert D et al. Community-acquired bacteremic urosepsis in the elderly patients: A prospective study of 34 consecutive episodes. J Urol 128:79, 1982; Kaye D. Urinary tract infections in the elderly. Bull NY Acad Med 56:209, 1980; and Ronald AR. Current concepts in the management of urinary tract infections in adults. Med Clin North Am 68:355, 1984; Sherman FT, Tucci V, Libow LS et al. Nosocomial urinary tract infections in a skilled nursing facility. J Am Geriatr Soc 28:456, 1980).

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Table I .15a. Recommended Antibiotics for Elderly Patients With Life-Threatening Infected Pressure Sores

Setting	Usual Pathogen(s)	Antibiotics*	Maximum Daily Dose (g)^2	Cost per Day ($)^3	Minimum Duration (Days)^4	Cost per Course ($)
Community	*Proteus sp.*	[Clindamycin] or	4.8	[$120.32] or	14	$1,684.48 or
Institution	*Escherichia coli*	[Metronidazole] or	4.0	[$44.64] or		$624.96 or
or	*Pseudomonas aeruginosa*	[Chloramphenical]		[$14.76]		$206.64
Hospital	*Staphylococcus aureus*	plus	See footnote	plus		plus
	Bacteroides fragilis	Aminoglycoside		$13.40-57.06		$315.00-798.84
	Polymicrobial	or	See footnote	or		or
		Antipseudomonal penicillins or	See footnote	$76.57-138.40		$1072-1937.60
				or		or
		[3rd-generation cephalosporins]	See footnote	$50.70-168.12		$709.80-2353.68

*See footnotes on Table I.13 for explanation of brackets [], and individual drugs (plus maximum daily dose and cost per day) contained in antibiotic subcategories.

(Data from Chow AW, Burdge DR. Pressure Sores. In: Gleckman RA, Gantz NM. eds. Infections in the elderly. Boston: Little Brown and Company, 1983: 319-41 and Bentley DW. Unpublished observations.

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Table I .15b. Recommended Antibiotics for Elderly Patients With Life-Threatening Total Parenteral Nutrition-Associated Septicemia.

Setting	Usual Pathogen(s)	Antibiotics*	Maximum Daily Dose (g)^2	Cost per Day ($)^3	Minimum Duration (Days)^4	Cost per Course ($)
Community	*Candida albicans*	Penicillinase-	See footnote	$46.20-74.76	10	$460.20-740.76
or	*Candida sp.*	resistant		or		or
Hospital	*Staphylococcus*	penicillins^9 or				500.70-1680.12
	epidermidis	[3rd-generation	See footnote	$50.70-168.12		or
	Gram-negative bacilli	cephalosporin] or		or		830.10
		[vancomycin] or	See footnote (2gm)	83.10 or		or
		amphotericin B	1 mg/kg (60kg)	20.98		209.80

*See footnote below and on Table I.13 for explanation of brackets [], and individual drugs (maximum daily dose plus cost per day) listed in the antibiotic subcategories. (Data from Bentley DW. Unpublished observations).

[9] Penicillinase-resistant penicillins include methicillin (12g; $74.76), oxacillin (12g; $62.88), nafcillin (9g; $46.20).

Table I.1b. Documentation of Antibiotic Use (HOSPITAL)

Table 7. Reasons for initiation of antimicrobial single-group courses, by hospital size, in 20 randomly selected hospitals in Pennsylvania.

Reason for initiation	No. of beds <150	151–300	>300	Total
Infectious disease	209 (61)	396 (62)	620 (54)	1,225
Operation or procedure	85 (25)	162 (26)	406 (35)	653
Fever	13 (4)	25 (4)	34 (3)	72
Symptoms other than fever; noninfectious diseases	35 (10)	40 (6)	56 (5)	131
Unknown	4 (1)	12 (2)	41 (4)	57
Total	346 (100)	635 (100)	1,157 (101)	2,138

NOTE. Data are given as number of antimicrobial single-group courses (percentage).

(Data from Shapiro M, Townsend TR, Rosner B, Kass EH. Use of antimicrobial drugs in general hospitals: Analysis of patterns of use. J Infect Dis 1979; 139:698-706)

Table 1.17

Characteristics of 173 Patients on Systemic Antibiotics for Acute Infection

		No. (%)
Patients	Total population	4378
	Total sampled	2238
	On antibiotics	173 (7.7%)
Age	Range	57-101
	Median	86
Sex	Female	75%
Payment	Medicaid	107 (61.9%)
	Private	63 (36.4%)
	Unknown	3 (1.7%)
Length of Stay (months)	Range	1-123
	Median	15
	Mean	26

(Data from Zimmer JG, Bentley, DW, Valenti WM, et al. Antibiotic Use in Nursing Homes: A Quality Assessment 1985, submitted for publication).

Table I.18

Suspected Site of Infection for Which Antibiotic was Ordered

Suspected Infection Site	Number	Percent
Urinary Tract	101	58.4%
Lower Respiratory Tract	33	19.1
Skin/Subcutaneous Tissue	8	4.6
Upper Respiratory Tract	3	1.7
Bone or Joint	2	1.2
Vagina	1	0.6
Oral Cavity	1	0.6
Could not be determined	24	13.9
Total	173	100.0%

Table I.19

The Physicians Responses to Suspected Infections Previous to the Antibiotic Order

All Infections (173) (Patient could have had more than one)	Number	Percent
Localizing Signs/Symptoms Recorded[a]	79	45.7%
Appropriate Culture Ordered[b]	66	38.2
Diagnosis Recorded by Physician[a]	61	35.3
Urinary Tract Infections (101)		
Urinalysis Ordered[b]	24	23.8%
Urine Culture Ordered[b]	58	57.4
Urinalysis, Culture, or Both	64	63.4
Lower Respiratory Infections (33)		
Chest Xray Ordered[b]	8	24.2%
Sputum Culture Ordered[b]	1	3.0
Xray, Culture, or Both	9	27.3

[a] Within 30 days prior to or on the day of the initial antibiotic order

[b] Within 14 days prior to or on the day of the initial antibiotic order

Table I.20

Evidence Available to the Physician at the Time of the Antibiotic Order

All Infections (173) (Patient could have had more than one)	Number	Percent
Localizing Signs/Symptoms Recorded[a]	79	45.7%
Positive Culture[b]	47	27.2
Fever of 100° or More,[c]	40	23.1
Elevated WBC Count[d]	9	5.2
Urinary Tract Infections (101)		
Positive Urinalysis[d]	20	19.8%
Positive Urine Culture[b]	42	41.6
Positive Urinalysis[d], Culture[b], or Both	52	51.5
Lower Respiratory Infections (33)		
Positive Chest Xray[e]	6	18.2%
Positive Sputum Culture[b]	1	3.0
Positive Xray[e] or Culture[b]	7	21.2

[a] Within 30 days prior to or on day of the initial antibiotic order

[b] Within 14 days prior to on on day of initial antibiotic order

[c] On the day of the initial antibiotic order

[d] Within 7 days prior to or on the day of the initial antibiotic order

[e] On or before the day of the initial antibiotic order

Table I.21

Systemic Antibiotic Ordered

By Site of Suspected Infection

	All Sites		Urinary Tract		Lower Resp. Tract	
	Number	Percent	Number	Percent	Number	Percent
Trimethoprim/Sulfamethoxazole	75	43.4%	55	54.5%	2	6.1
Ampicillin or Amoxicillin	32	18.5	8	7.9	19	57.6
Nitrofurantoin	14	8.1	14	13.9	0	0
Cephalexin	12	6.9	5	5.0	1	3.0
Sulfonamides	12	6.9	12	11.9	0	0
Tetracycline	9	5.2	0	0	4	12.1
Erythromycin	5	2.9	0	0	4	12.1
Methenamine mandelate	4	2.3	4	4.0	0	0
Penicillin V	2	1.2	1	1.0	0	0
Other (one each)*	8	4.6	2	2.0	3	9.1
Total	173	100%	101	100.0%	33	100.0%

* Dicloxicillin and nalidixic acid for urinary tract; cefazolin, cephradine and INH for lower respiratory tract; gentamicin, chloramphenicol and rifampin for other sites.

Table I.22 Demographics Regarding Financial Considerations Health and Medication Consumption

Table 2-1 U.S. Nursing Home Population. Present and Projected

Year	*Number of residents*
1980	1.3 million
2000	1.95 million
2030	2.95 million

Source: Reprinted from *Long term care: Background and future directions* (Publication No. HCFA 81-20047) by the U.S. Health Care Financing Administration, Washington, D.C., 1981

Table 2-2 Discharge Rate from Short-Stay Hospitals by Patient Age

Age	*Discharges per 1,000 population*
Total population	164
65 and older	382
85 and older	507

Source: Reprinted from *Need for long term care: Information and issues. A chartbook of the Federal Council on the Aging, 1981* (Publication No. OHDS 81-20704) by the Office of Human Development Services, 1981

Table 2-3 Out-of-Pocket Expenses for Prescribed Medicines: Percent Distribution of Persons with and without Prescribed Medicines by Intervals of Out-of-Pocket Expense

Age of patient	*None*	*$1–49*	*$50-99*	*$100-249*	*$250 or more*
Under 6	10.6	51.0	3.4	0.4	0.0
6 to 18	7.7	34.7	1.6	0.5	0.0
19 to 24	6.9	40.1	3.2	0.8	0.1
25 to 54	7.9	41.7	5.8	3.2	0.5
55 to 64	6.9	40.5	10.2	9.3	2.2
65 or older	6.6	34.7	14.8	15.7	3.3
Total population	8.0	38.8	5.7	3.8	0.8

Source: Reprinted from *Prescribed medicines: Use, expenditures, and source of payment* (Data Preview 9. National Health Care Expenditure Study, U.S. Department of Health and Human Services, Publication No. (PHS) 82-3320) by J.A. Kasper, 1982.

Table 2-4 Use of Prescribed Medicines: Percent of Adults in the United States with Prescribed Medicines in 1977

Age in years	*Percentage with at least one prescribed medicine*
19 to 24	53.2
25 to 54	58.1
55 to 64	66.1
65 or older	75.2
Total population	58.2

Source: Reprinted from *Prescribed medicines: Use, expenditures, and source of payment* (Data Preview 8. National Health Care Expenditure Study, U.S. Department of Health and Human Services, Publication (PHS) 82-3320) by J.A. Kasper, 1982.

Table 2-5 Use of Prescribed Medicines: Mean Number of Prescribed Medicines per Noninstitutionalized Person and per Person with at Least One Prescribed Medicine, by Patient Age

Age in years	*Prescriptions per person*	*Prescriptions per person with at least one prescribed medicine*
19 to 24	2.6	4.9
25 to 54	4.2	7.0
55 to 64	8.2	11.9
65 or older	10.7	14.2
Total population	4.3	7.5

Source: Reprinted from *Prescribed medicines: Use, expenditures, and source of payment* (Data Preview 8. National Health Care Expenditure Study, U.S. Department of Health and Human Services, Publication No. (PHS) 82-3320) by J.A. Kasper, 1982.

Table II.23. Drug Categories Most Frequently Prescribed For Out Patients Aged 45 Years and Older

Table 9.2. Rank Within Age Groups for Drug Categories Used Most Often by People Aged 45 and Older

USC Category	Age Group				
	0–44	45–54	55–64	65–74	75+
Systemic antiarthritics	8	1	2	1	2
Beta-blockers	20	2	1	2	6
Thiazide and related diuretics	28	3	3	3	4
Digitalis preparations	99	34	9	4	1
Potassium-sparing diuretics	49	5	4	5	5
Other oral diuretics (eg, furosemide)	78	18	8	6	3
Other antihypertensives (eg, methyldopa)	73	8	5	8	8
Nitrite/nitrate coronary vasodilators	*	16	7	7	7
Benzodiazepine tranquilizers	14	4	6	10	12
Diabetes therapy, oral	100	17	11	9	9
Codeine and combinations, oral analgesics	10	6	9	15	16
Plain corticoids, oral	15	12	13	14	15
Xanthine bronchodilators	18	23	14	11	13
Diabetes therapy, insulin	56	19	12	12	21
Tricyclic and related antidepressants	17	7	15	20	27

Source: *National Disease and Therapeutic Index*, IMS America, Ltd, 1982.

*Not in top 100.

(Data from Baum C, Kennedy DL, Forbes MB. Drug Utilization in the geriatric age group. In: Moore SR, Teal TW, eds. Geriatric drug use - clinical and social perspectives. New York: Purgamon Press, 1985: 63-69)

Table I.24. Drug Use and Expenditures in 1982.

Table 1.—Distribution of Overall Drug use by Age and Sex*

	% US Population	% Total Patient Visits to Physicians	% Total Drug Mentions
Patient age, yr			
0-2	8	7	8
3-9	10	6	5
10-19	16	8	7
20-29	18	14	12
30-39	16	15	11
40-49	10	10	9
50-59	10	11	13
60-69	8	13	16
70+	8	17	22
Patient sex			
M	49	40	40
F	51	60	60

*Data from the *National Disease and Therapeutic Index, 1982.* Population figures were based on US resident population as of July 1, 1982.

Table 3.—Cost to Drugstores and Hospitals for Ethical Pharmaceuticals* by Major Therapeutic Classes

Uniform System of Classification Class	Dollars in Millions		% Combined Market
	Drugstores	Hospitals	
Anti-infectives administered for systemic effects	873.0	1,009.3	13.6
Cardiovascular drugs	1,496.8	232.7	12.5
Psychotherapeutics	879.2	132.2	7.3
Antiarthritics	780.5	64.8	6.8
Analgesics	666.3	96.3	5.5
Hormones	490.3	136.4	4.6
Antispasmodics and other gastrointestinal/genitourinary agents	457.2	96.9	4.0
Contraceptives	540.9	8.5	4.0
Diuretics	457.4	44.8	3.7
Cough/cold preparations	481.4	18.8	3.6
Vitamins	416.8	26.4	3.2
Ophthalmic preparations	[illegible]	57.8	3.1
Dermatologicals	329.3	53.8	2.8
[illegible]	[illegible]	[illegible]	2.6
Bronchial therapy	246.9	53.2	2.2
[illegible]	[illegible]	62.1	2.1
Total, 16 Classes	8,996.6	2,117.7	80.2†
[illegible]	[illegible]	[illegible]	[illegible]

*Ethical over-the-counter drugs are included (ie, those promoted to health professionals).

†Column totals 80.4% because of rounding error. Data from the *U.S. Pharmaceutical Market—Drug Store and Hospital Purchases, 1982.*

(Data from Baum C, Kennedy DL, Forbes MB, Jones JK. Drug use and expenditures in 1982. JAMA 1985; 253: 382-386).

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Table I.26. Changing Patterns of Hospital Infections and Antibiotic Use: Prevalence Surveys in a Community Hospital

Table 4.—Antimicrobial Agents Being Administered to 464 Hospitalized Patients at LDS Hospital, August 1979

	No. (%) Alone	No. (%) With Others	Total (%)
Antimicrobial agent			
Penicillin G, penicillin V	7(1.5)	3(0.6)	10(2.2)
Ampicillin	20(4.3)	3(0.6)	23(5.0)
Penicillinase-resistant penicillins	3(0.6)	2(0.4)	5(1.1)
Carbenicillin, ticarcillin	0	4(0.9)	4(0.9)
Cephalosporins*	68(14.7)	11(2.4)	79(17.0)
Cefamandole, cefoxitin	16(3.4)	3(0.6)	19(4.1)
Erythromycin	2(0.4)	0	2(0.4)
Clindamycin	1(0.2)	7(1.5)	8(1.7)
Tetracycline	4(0.9)	0	4(0.9)
Chloramphenicol	2(0.4)	1(0.2)	3(0.6)
Gentamicin	2(0.4)	14(3.0)	16(3.4)
Tobramycin	1(0.2)	2(0.4)	3(0.6)
Amikacin	0	2(0.4)	2(0.4)
Nitrofurantoin	4(0.9)	1(0.2)	5(1.1)
Sulfonamides	8(1.7)	3(0.6)	11(2.4)
Others	2(0.4)†	3(0.6)‡	5(1.1)
Patients receiving 1 antimicrobial agent	...	...	142(30.6)
Patients receiving 2 antimicrobial agents	...	...	24(5.0)
Patients receiving 3 antimicrobial agents	...	...	4(0.9)
Total No. of patients receiving antimicrobial agents	...	...	170(36.6)

*Includes cephalexin, cephradine, cephalothin, cephapirin, cefazolin.
†Metronidazole 1, and methenamine hippurate, 1.
‡Nystatin, 2.

Table 5.—Comparison of Relevant Data From Two Surveys at LDS Hospital

	1971 (%)*	1979 (%)
Total No. of patients	560(100)	464(100)
Medical	179(31.6)	106(22.8)†
Surgical	367(68.4)	358(77.2)†
Patients with infections	107(19.0)	73(15.7)
Community-acquired infections	60(10.6)	43(9.3)
Hospital-acquired infections	48(8.5)	32(6.9)
Hospital-acquired infection sites		
Lower respiratory tract	9(1.7)	8(1.7)
Urinary tract	21(3.7)	14(2.9)
Skin and subcutaneous tissue	2(0.4)	1(0.2)
Wounds	12(2.1)	8(1.7)
Others	11(1.9)	13(2.8)
Patients receiving antimicrobials	130(23.0)	170(36.6)†
Without bacterial infection	63(11.3)	112(24.1)†
Bacterial infections cultured	N/Total (%)	N/Total (%)
Community-acquired infections	32/47(68.1)	39/45(86.7)
Hospital-acquired infections	38/44(86.4)	34/38(89.5)
Bacterial isolates from hospital-acquired infections		
Staphylococcus aureus	3/58(5.2)	3/45(6.7)
Gram-negative bacilli	35/58(60.3)	31/45(68.9)
Others	20/58(34.5)	10/45(22.2)
Patients with indwelling bladder catheters	64/560(11.5)	84/464(18.1)‡
Patients with urinary tract infections	10/64(15.6)	11/84(13.1)
Patients with intravenous or arterial catheterization	19/560(3.4)	38/464(8.2)‡
Patients with catheter infections	0/11(0.0)	0/38(0.0)

*From Moody and Burke.
†Differences from 1971 survey are significant ($P < .005$) on basis of χ^2.
‡Differences are significant ($P < .001$).

(Data from Stevens GP, Jacobson JA, Burke JP. Changing patterns of hospital infectio and antibiotic use: prevalence surveys in community hospital. Arch Intern Med 1981; 141:587-92)

Table I.27. Use of Antimicrobial Drugs in General Hospitals.

Table 2. Age distribution of patients receiving antimicrobial drugs (AMD) in 20 randomly selected hospitals in Pennsylvania.

Age (years)	Total no. of patients	No. (%) of patients receiving AMD
<14	933	203 (22)
15–24	768	184 (24)
25–34	701	156 (22)
35–44	514	133 (26)
45–54	645	181 (28)
55–64	649	222 (34)
65–74	588	217 (37)
75–84	380	148 (39)
85+	103	50 (49)
Unknown	9	2 (0)
Total	5,288	1,496 (28)

Table 5. Frequency distribution of antimicrobial courses, by drug group, in 20 randomly selected hospitals in Pennsylvania.

	Antimicrobial courses		
Drug group	No.	Percentage ± SEP	TPE ± 2 SEP × 10^3
Ampicillin	467	22.0 ± 1.8	139 ± 11
Cephalosporins	386	18.0 ± 1.7	115 ± 11
Benzylpenicillins	304	14.0 ± 1.5	90 ± 10
Tetracyclines	276	13.0 ± 1.4	82 ± 9
Sulfonamides	134	6.0 ± 0.5	40 ± 3
Erythromycins	109	5.0 ± 0.5	32 ± 3
Nitrofurantoin	80	4.0 ± 0.4	24 ± 3
Gentamicin	73	3.0 ± 0.4	22 ± 3
Penicillinase-resistant penicillins	60	3.0 ± 0.4	18 ± 3
Kanamycin	51	2.0 ± 0.3	15 ± 2
Clindamycin	48	2.0 ± 0.3	14 ± 2
Methenamine mandelate	35	2.0 ± 0.3	10 ± 2
Lincomycin	27	1.0 ± 0.2	8 ± 1
Carbenicillin	20	0.9 ± 0.2	6 ± 1
Streptomycin	19	0.9 ± 0.2	6 ± 1
Neomycin	19	0.9 ± 0.2	6 ± 1
Chloramphenicol	16	0.8 ± 0.2	5 ± 1
Nalidixic acid	8	...	...
Nitrofurazone	1	...	...
Furazolidone	1	...	...
Vancomycin	1	...	...
Unknown	5	...	...
Total	2,138	100	...

NOTE. SEP = standard error of the proportion. TPE = target population estimate.

(Data from Shapiro M, Townsend TR, Rosner B, Kass EH. Use of antimicrobial drugs in general hospitals: Analysis of patterns of use. J Infect Dis 1979; 139:698-706)

Table I.28a

Table 6-8
Drugs Ordered on a PRN Basis for Day Treatment Center Patients

Category	Percent of drugs PRN
Antihistamines	50
Autonomic agents	25
Cardiovascular drugs	17
CNS drugs	47
Cough and cold	95
Gastrointestinal	100
Skin preparations	100

Source: Boykin, S.P., Burkhart, V.P., and Lamy, P.P. Drug use in a day treatment center. *Am J Hosp Pharm.* 35:155, 1978.

Table 6-9
Most Frequently Used Drugs in Skilled Nursing Facilities

Drug category	Percent patients receiving
Cathartics	53.3
Analgesics and antipyretics	47.7
Tranquilizers	44.8
Diuretics	33.8
Vitamins	33.3
Sedatives and hypnotics	33.2
Cardiac drugs	28.9
Skin and mucous membrane	17.7
Anti-infectives	16.9
Antacids and absorbents	14.2
Antihistamines	13.8
Hypotensives	12.4
Eye, ear, nose, and throat	11.8
Spasmolytics	11.4
Insulin and antidiabetic agents	11.1
Electrolyte replacements	9.9

Source: Long-term care facility improvement study. Introductory Report. Office of Nursing Home Affairs. DHEW Publ. No. (OS) 76-50021. Rockville, Md., 1975.

(Data from Lamy PP. Healthcare expenditures and drugs. In: Lamy PP. Prescribing for the elderly. Littleton, Mass., PSG Publishing, 1980; 89-108)

Table I.28b

Table 6-11
Prescription Drug Use in Skilled Nursing Facilities

Drug	Percent of patients
Psychotropic	51.3
Cardiac, antihypertensives, diuretics	13.0
Vasodilators	11.5
Insulin	10.5
Antidepressants	8.6
Estrogens	4.4

No. of Patients: 283,915
No. of Prescription Drugs: 1,731,360
Av. No. of Rx Drugs/Patient: 6.1
Source: Long-term care facility improvement campaign. Monograph No. 2. Physicians' drug prescribing patterns in skilled nursing facilities. U.S. DHEW. PHS. Office of Long Term Care. DHEW Publ. No. (OS) 76-50050. Washington, D.C.: U.S. Government Printing Office. 1976.

Table 6-14
Conditions for Which Drugs Were Most Frequently Prescribed

Condition	All ages	45–64 years	65 years and over
High blood pressure	6.8	10.9	13.2* (5.80)†
Heart conditions	5.4	7.8	12.4 (5.20)
Arthritis and disorders of bones and joints	3.8	5.4	7.5 (6.40)
Mental and nervous conditions	7.5	10.3	7.1 (5.20)
Other digestive system conditions	4.5	4.8	5.3 (4.40)
Other disorders of circulatory system	1.9	1.9	4.7 (6.90)
Diabetes	2.8	4.4	4.6 (6.30)
Eye or ear conditions	3.9	2.4	3.4 (4.60)

*Percent Distribution.
†Av. cost per prescription in 1973.
Source: Out-of-pocket cost and acquisition of prescribed medicines. U.S. 1973. DHEW Publ. No. (HRA) 77-1542. Rockville, Md.: National Center for Health Statistics. 1977.

(Data from Lamy PP. Healthcare expenditures and drugs. In: Lamy PP. Prescribing for the elderly. Littleton, Mass., PSG Publishing, 1980; 89-108)

Table I . 29. _distribution of Most Frequent Oral Antibiotics Prescribed in an Ambulatory-Care Setting by Age Group

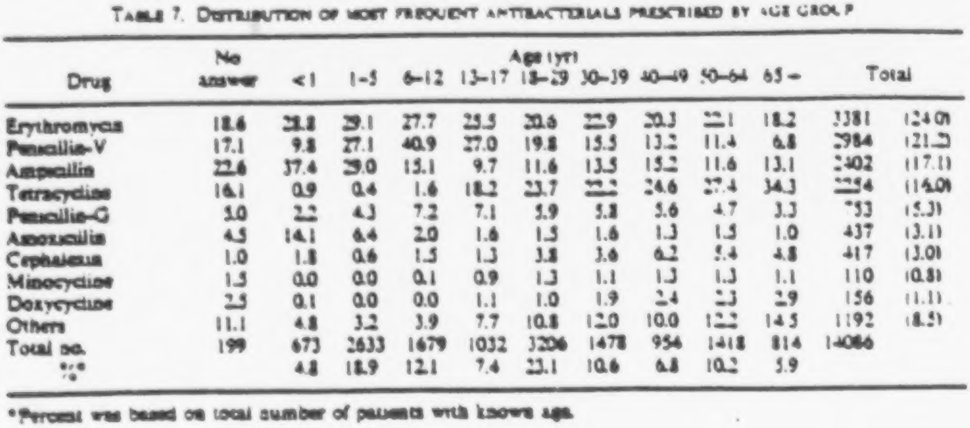

TABLE 7. DISTRIBUTION OF MOST FREQUENT ANTIBACTERIALS PRESCRIBED BY AGE GROUP

Drug	No answer	Age (yr) <1	1–5	6–12	13–17	18–29	30–39	40–49	50–64	65 –	Total	
Erythromycin	18.6	28.8	29.1	27.7	23.5	20.6	22.9	20.3	22.1	18.2	3381	(24.0)
Penicillin-V	17.1	9.8	27.1	40.9	27.0	19.8	15.5	13.2	11.4	6.8	2984	(21.2)
Ampicillin	22.6	37.4	29.0	15.1	9.7	11.6	13.5	15.2	11.6	13.1	2402	(17.1)
Tetracycline	16.1	0.9	0.4	1.6	18.2	23.7	22.2	24.6	27.4	34.3	2254	(16.0)
Penicillin-G	5.0	2.2	4.3	7.2	7.1	5.9	5.8	5.6	4.7	3.3	753	(5.3)
Amoxicillin	4.5	14.1	6.4	2.0	1.6	1.5	1.6	1.3	1.5	1.0	437	(3.1)
Cephalexin	1.0	1.8	0.6	1.5	1.3	3.8	3.6	6.2	5.4	4.8	417	(3.0)
Minocycline	1.5	0.0	0.0	0.1	0.9	1.3	1.1	1.3	1.3	1.1	110	(0.8)
Doxycycline	2.5	0.1	0.0	0.0	1.1	1.0	1.9	2.4	2.3	2.9	156	(1.1)
Others	11.1	4.8	3.2	3.9	7.7	10.8	12.0	10.0	12.2	14.5	1192	(8.5)
Total no.	199	673	2633	1679	1032	3206	1478	954	1418	814	14086	
%*		4.8	18.9	12.1	7.4	23.1	10.6	6.8	10.2	5.9		

*Percent was based on total number of patients with known age.

(Data from Borden EK, Lee JG. A methodologic study of post-marketing drug evaluation using a pharmacy-based approach. J Chron Dis 1982; 35: 803-16)

Table I.30. Physicians' Drug Prescribing Patterns in Skilled Nursing Facilities.

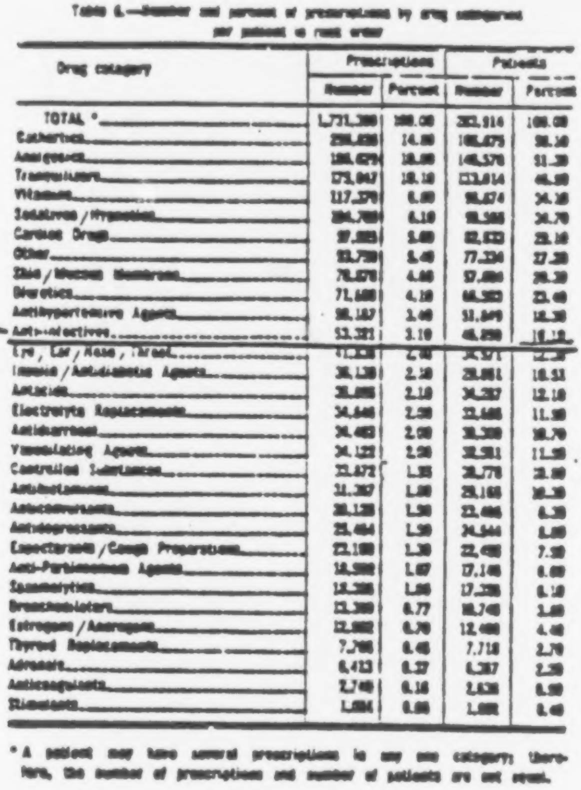

Table 6.—Number and percent of prescriptions by drug categories per patient in rank order

Drug category	Prescriptions		Patients	
	Number	Percent	Number	Percent
TOTAL *	1,731,3[illegible]	100.00	283,916	100.00
Cathartics	[illegible]	14.80	108,675	38.10
Analgesics	186,679	10.80	145,570	51.30
Tranquilizers	175,047	10.10	133,814	46.90
Vitamins	117,370	6.80	98,874	34.10
Sedatives/Hypnotics	104,780	6.10	98,566	34.70
Cardiac Drugs	97,085	5.60	82,033	28.10
Other	93,730	5.40	77,334	27.20
Skin/Mucous Membranes	78,078	4.60	57,000	20.30
Diuretics	71,600	4.10	66,523	23.40
Antihypertensive Agents	58,187	3.40	51,849	18.30
Anti-infectives	53,321	3.10	46,250	16.10
Eye, Ear, Nose, Throat	41,[illegible]	2.40	34,571	[illegible]
Insulin/Antidiabetic Agents	36,130	2.10	29,881	10.51
Antacids	35,895	2.10	34,337	12.10
Electrolyte Replacements	34,646	2.00	32,668	11.50
Antidiarrheals	34,483	2.00	30,300	10.70
Vasodilating Agents	34,122	2.00	32,581	11.50
Controlled Substances	23,472	1.35	[illegible]	[illegible]
Antihistamines	31,387	1.80	29,168	10.30
Anticonvulsants	26,125	1.50	23,466	8.30
Antidepressants	25,404	1.50	24,544	8.60
Expectorants/Cough Preparations	23,180	1.30	22,498	7.30
Anti-Parkinsonism Agents	18,500	1.07	17,146	6.00
Spasmolytics	18,336	1.06	17,336	6.10
Bronchodilators	13,300	0.77	10,740	3.80
Estrogens/Androgens	12,882	0.70	12,480	4.40
Thyroid Replacements	7,786	0.45	7,718	2.70
Adrenals	6,413	0.37	6,387	2.30
Anticoagulants	2,740	0.16	2,636	0.90
Stimulants	1,084	0.06	1,082	0.40

* A patient may have several prescriptions in any one category; therefore, the number of prescriptions and number of patients are not equal.

(Data from U.S. Department of Health, Education and Welfare. Public Health Service, Office of Long Term Care. Physician's Drug Prescribing Patterns in Skilled Nursing Facilities: Long Term Care Facility Improvement Campaign Monograph #2. DHEW Pub. No. (05)76-50050. Washington, D.C., US Government Printing Office, June 1975; 1-6,14,43,48)

Table I. 31. Physician's Drug Prescribing Patterns in Skilled Nursing Facilities

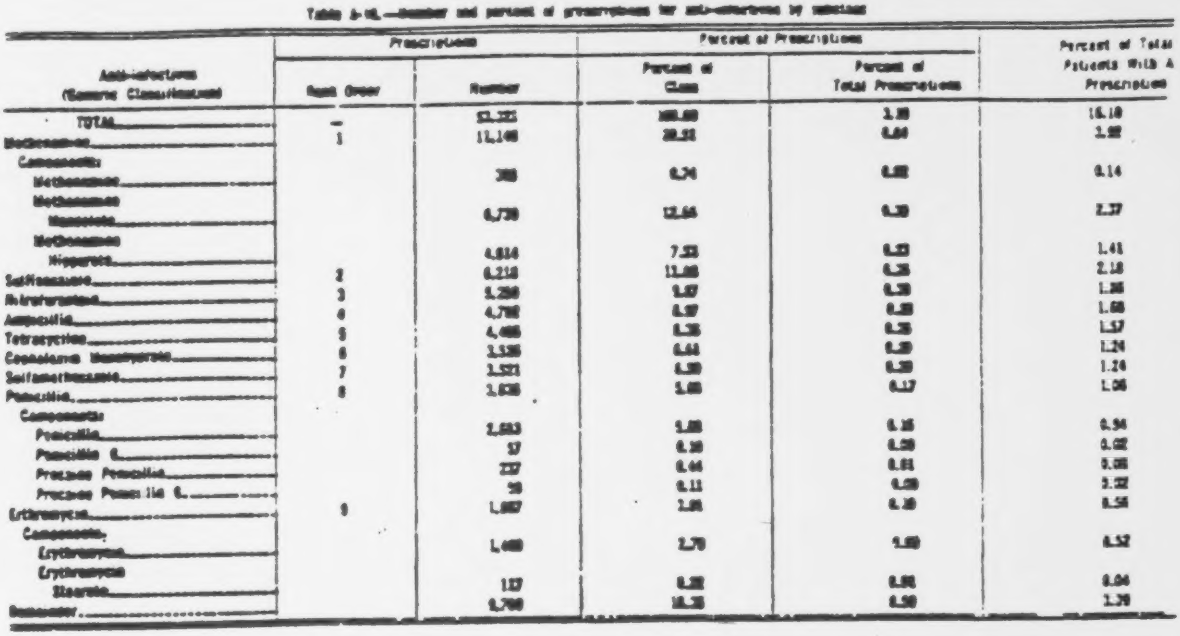

Table [illegible].—Number and percent of prescriptions for anti-infectives by subclass

Anti-infectives (Generic Classification)	Prescriptions		Percent of Prescriptions		Percent of Total Patients With A Prescription
	Rank Order	Number	Percent of Class	Percent of Total Prescriptions	
TOTAL	—	53,325	100.00	3.18	16.10
Methenamine	1	11,148	20.91	0.66	3.92
Components:					
Methenamine		398	0.74	0.02	0.14
Methenamine Mandelate		6,730	12.66	0.39	2.37
Methenamine Hippurate		4,014	7.53	0.23	1.41
Sulfisoxazole	2	6,218	11.66	0.36	2.18
Nitrofurantoin	3	5,250	9.87	0.31	1.86
Ampicillin	4	4,788	8.97	0.28	1.68
Tetracycline	5	4,466	8.36	0.26	1.57
Cephalexin Monohydrate	6	3,536	6.64	0.20	1.24
Sulfamethoxazole	7	3,521	6.59	0.20	1.24
Penicillin	8	3,026	5.68	0.17	1.06
Components:					
Penicillin		2,683	5.03	0.15	0.94
Penicillin G		57	0.10	0.00	0.02
Procaine Penicillin		237	0.44	0.01	0.08
Procaine Penicillin G		58	0.11	0.00	0.02
Erythromycin	9	1,607	3.05	0.10	0.56
Components:					
Erythromycin		1,480	2.78	0.09	0.52
Erythromycin Stearate		127	0.22	0.01	0.04
Remainder		9,700	18.35	0.58	3.39

(Data from U.S. Department of Health, Education and Welfare. Public Health Service, Office of Long Term Care. Physician's Drug Prescribing Patterns in Skilled Nursing Facilities: Long Term Care Facility Improvement Campaign Monograph #2. DHEW Pub. No. (05)76-50050. Washington, D.C., U.S. Government Printing Office, June 1976; 1-6, 14, 43, 48)

Table I . 32a. Final Report on Special Data Systems

Service	Specific Data System	Data Available for OTA Report	Comments Problems
National Center For Health Statistics 3700 E.W. Highway Hyattsville, MD 20782	National Ambulatory Medical Care Survey (NSMCS) Contact: Gloria Gardocki, Ph.D., Health Statistician 1-301-436-7132	- 1980-81 from a sample of 9,000 visits to a sample of 6,000 physicians in office-based private practice - Physicians' first, second and/or third diagnoses as per ICD 9 CM code - Number and names of the specific drugs prescribed but the number of visits for the elderly is so small that any information about specific drugs would be meaningless. - Can provide cross-tabulation from disease to age (65-79 and 80+) and type of antibiotic (by subcategory). But most of the statistics that emerged were unrealistic, lending to the conclusions that 65+ is the best age category to use.	-Final search indicates that low frequency of use is below NCHS standards of statistical reliability.

*See additional materials submitted to H. Shaman

Table I.32b. Final Report on Special Data Systems (Continued)*

Service	Specific Data System	Data Available for OTA Report	Comments/ Problems
National Center For Health Statics 3700 E.W. Highway Hyattsville, MD 20782	National Medical Care Utilization and Expenditure Survey (NMCUES) Contact: Michele Chyba, Statistician 301-436-7100	- Information from respondents in 10,000+ households (1980). - Limited information on hospital stay, more information on emergency room visits or hospital out-patient visit. - Administrative records, (Medicaid eligibility files, Medicaid claims and provider files, Federal Medicare claim files) merged with household data from persons or from individual healthcare events. - Responder lists conditions which are coded from Administrative records by ICD 9 codes - Specific drugs identified for condition. - Can provide cross-tabulation from condition (disease) to age and type of antibiotic (by subcategory).	- Data not physician-verifiable. - Final search for specific diseases demonstrat frequencie below leve for which data is reliable, i.e., < than 300 episodes o bacterial pneumonia. -NMCUES doe not recomm that the data be use

*See additional materials submitted to H. Shaman

Table I .32c. Final Report on Special Data Systems (Continued)*

Service	Specific Data System	Data Available for OTA Report	Comments/ Problems
National Center For Health Statistics 3700 E.W. Highway Hyattsville, MD 20782	National Hospital Discharge Survey Contact: Mary Moien, Chief, Hospital Care Statistics Branch 301-436-7125	- Information from data abstracted from a sample of approximately 200,000 records from a sample of 500 non-Federal short stay hospitals. - 1983 Survey has up to seven discharge diagnoses as per ICD 9 CM code. - Can provide estimated number (in 1000's) of discharges with specific infectious diseases cross-tabulated for age 65+	No informati on drugs.

*See additional materials submitted to H. Shaman

Table I.32d. Final Report on Special Data Systems (Continued)*

Service	Specific Data System	Data Available for OTA Report	Comments Problems
National Center For Health Statistics 3700 E.W. Highway Hyattsville, MD 20782	National Nursing Home Survey (NNHS) Contact: Alvin Sirrocco, Esther Hing, Statisticians, c/o Long Term Care Statistics 301-436-8830	- Information on nursing home residents personal health characteristics based on interviews with staff in a sample of 2,100 nursing homes -Can provide out-of-stock narrative for: . Number and percent of residents by category of medication (includes antibiotics) . Percent distribution by type of category of medication according to sex amd age (65-74 75-84, 85+).	-Informatio on drugs, including antibiotic is based o 1973-74 data. -Number and percent of residents by categor of medicin received according chronic condition or primary diagnosis last examination. No mention of four acute specific infections.

THIS DESCRIPTION APPLIES ONLY TO DA
FROM THE 1973-74 NNHS

*See additional materials submitted to H. Shaman

Table I .32e. Final Report on Special Data Systems (Continued)*

Service	Specific Data System	Data Available for OTA Report	Comments/ Problems
Health Care Finance Administration (HCFA) [2C-14 Oak Meadows] 6325 Security Blvd. Baltimore, MD 21027	HCFA Medicare data, Contact: Charles Helbing, Supervisor of Statistics 301-597-1420	- Information from Medicare records from a 20% sample (2M) of 10M discharges from non-Federal short-stay hospitals. - 1983 and 1984 data have principle diagnosis and 4 additional ones coded as per ICD 9 CM. - Can provide estimated number (in 1000's) of discharges with specific infectious diseases cross-tabulated by ages (65-79, 80+) - Additional information available: . total pharmacy charges per dx. . average total charges per stay. . % pharmacy charges per stay. . average length of stay.	- Pharmaceutical costs are for total aggregat cost. Informat on antibiotics not in stay record. Estimates of proportion fo antibiotics a possible but n reliable.

*See additional materials submitted to H. Shaman

Table I .32f. Final Report on Special Data Systems (Continued)*

Service	Specific Data System	Data Available for OTA Report	Comments/Proble
IMS America, Ltd. Butler and Maple Ambler, PA 19002	National Disease Therapeutic Index (NDTI) Contact: Amy Abrams, Director, Product Management 215-283-8869	- Information from a panel of ~ 2,000 private office-based physicians. - Every contact with patient during a specified two-day period. - Includes all drug mentions during MD-patient contact, drugs administered (injections) and a fraction of hospital drug use (17% of contacts). - Can provide 1984 data on: . Total and % of patient visits/contacts for ages 65-74, 75-84, 85+. . Specific diagnoses coded by ICD 7 CM. . Specific drugs by subcategory includes antibiotics. . Can provide cross-tabulation from diagnosis to age to subcategory of antibiotics.	- Drug utilizatio data excludes refill prescriptions. - Will not releas data from Natio Prescription Au (NPA) which is necessary to es mate overall ou patient exposur for an age grou - Contacts occur i the hospital but data from sales to hospitals bas on U.S. pharmaceutical market-hospitals (USH) and must be obtained elsewhe - Actual utilizati (and expenditure will require est mates based on "average" daily dose and "recommended" duration of trea ment. - Draft of report must be reviewed prior to submission.

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*See materials submitted to H. Shaman; OTA may wish to followup directly with service.

Table I.32g. Progress Report on Special Data Systems (Continued*)

Service	Specific Data System	Data Available for OTA Report	Commments/Problems
Health Information Designs 1616 N. Fort Myer Dr. Suite 1420 Arlington, VA 22209	Compass Data Base, Contact: Lee Morse, Pharm. B., President 703-528-2032	-Information from Medicaid paid claims for 10 state agencies on ~ 6M persons and ~ 1.5M short-term hospital and long-term care beds. -Data is chronologic, longitudinal and prospective. -Specific diagnoses as per ICD 9 CM codes. -Specific drugs by individual code or subgroupings including antibiotics. -Can provide cross-tabulations from disease (specific infections) by ages (65-74, 75-84, 85+) and type of antibiotic (by subcategory).	-Drug data is not available from hospitals because costs are not reimbursed by Medicaid. -Data that can be provided free of charge limited to materials already available. Overhead charges a Federal contractor requires that we be charge for services rendered.

STUDIES OF HOSPITALIZATION OF NURSING HOME RESIDENTS FOR ACUTE INFECTION

Author and Location	Elements of Study Design	Summary of Findings
A. Irvine et al, 1984 Minneapolis	Medical record review to identify, describe and compare hospitalizations among elderly nursing home patients (N=900) and outpatients (N=1700) under the care of a physician group, during 6 month period (1/81-6/81).	Infections responsible for 35 of 128 (27%) hospitalization from nursing homes and 38 of 320 (12%) hospitalization of outpatients. Data on specific infections include
B. Trench et al, 1985 Baltimore	Medical record review of all hospitalizations among 229 patients residing in a single nursing home, under care of Geriatric Medicine Division of Johns Hopkins School of Medicine, during one year period (9/83-8/84).	Infections responsible for 18 of 60 (30%) hospitalizations. Data on specific infections include
C. Mott and Barker, 1985 Rochester	Mecial record review to describe and analyze disposition of acute medical episodes among 110 nursing home patients under care of medical group during 7-year period (1976-1983)	Infections responsible for 73 of 130 130 (56%) hospitalizations. Data on specific infections include
D. Gordon et al, 1985 Los Angeles	Medical record of all hospitalizations among 373 residents of a multi-level of care nursing home, under care of one full-time primary care physicians, during 4-year period (10/77-9/81)	503 admissions among 373 residents during four year study period. Limited data on role of fever and of specific infections.
E. Brown & Thompson, 1979	Medical record review on 1256 patients admitted to 9 extended care facilities during 1973 to determine factors in making decision to treat or not to treat acute fever, during a 2-year period.	Fever (101-102°) occurred in 190 patients over two years. Active treatment, including antibiotics and hospitalization provided in 109 (57%) of these. Limited data on specific infections
F. Gillick & Steel, 1983 Boston	Concurrent observation of patients $\geq$ 70 years presenting to Boston City Hospital during 4-period (12/81-3/87) to compare diagnoses, patient characteristics and outcomes for those from 3 settings: Home, Nursing Home and Chronic-care Hospital	Fever ($\geq$ 102°) present as follows -Patients from home 4/222 (2%) -Patients from N. home 9/52 (17%) -Patients from chronic hospital 3/10 (30%) No data on specific infections.
G. Gabow et al, 1985 Denver	Concurrent observation and comparison of consecutive admissions of elderly nursing home and community residents for four university-affiliated hospitals, during 6-month period.	Fever and/or sepsis responsible for 32 of 98 (32%) of nursing home admissions compared with 2 of 88 (3%) of community admissions.

ANTIBIOTICS USE IN THE ELDERLY

TASK II

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TASK II

DEFINITIONS for the purpose of this paper

A competent patient is one who satisfies the criteria of maturity and comprehension. Such a patient is an adult 18 years or older (or, if younger, the parent of a child, married or divorced, or otherwise emancipated) and can comprehend the nature and severity of the illness, the prognosis, the therapeutic options which are available, and the probable results of these options; such a person can make informed and deliberate choices about treatment.

An incompetent patient fails the criteria of maturity and comprehension and is unable to make informed and deliberate choice about treatment.

A surrogate is a family member or a "significant other" established either by longstanding association or by durable power of attorney. The surrogate must be competent, must know the patient well and be able to represent his or her wishes, and must possess a judgment of the patient's welfare unimpaired by a conflict of interest.

ASSUMPTIONS

Health care professionals act for the good of the patient.

Physicians are responsible for making medical decisions: for diagnosis, prognosis, and choice of therapy. Competent patients have the right to refuse treatment, even potentially life-saving treatment. This refusal is not to be confused with suicide.[1]

Although caretakers must be especially cautious about the effects of depression in the elderly, all patients are presumed competent until demonstrated to be otherwise.

Any serious infection in an elderly person who is well or is chronically ill but stable is potentially life threatening.

In this task we will not consider important public health issues such as the increased resistence to bacteria from antibiotic use ("herd immunity").

For the purposes of this task we will assume that antibiotics have only mild or no toxicity and that the course of treatment is seven to ten days.

REVIEW OF THE LITERATURE

Standard treatment

The professional standard of treatment is the routine administration of antibiotics for infection. The Critical Care Committee of the Massachusetts General Hospital[2] in its distinction of four levels of care placed antibiotic therapy in the third category, general medical care. This assumption is adopted by Wanzer et al in their discussion of "The Physician's Responsibility toward Hopelessly Ill Patients."[3] Routine administration of antibiotics is also implicit in Hilfiker's discussion of his compromise decision to use intramuscular antibiotics without a workup for an elderly comatose febrile patient who had expressed a desire not to be kept alive before her last stroke.[4] Because there are no legal issues and no ethical dilemmas arising from this professional standard of treatment, the legal and medical-ethical literature on antibiotic use is minimal. Kapp cautions against the rationing of "normal" health care: "...it is neither legally nor ethically permissible under our present scheme of things for physicians to withhold or withdraw minimally adequate services from an older patient solely on the basis of the physician's cost determinations or exigencies."[5] (p.182).

Extraordinary treatment

There is evidence, however, that in some circumstances antibiotic therapy is regarded as extraordinary treatment. Brown and Thompson in their 1979 study of nontreatment of fever in extended-care facilities found that 43% of febrile patients were not given antibiotics. Although they question of the "heroic" status of antibiotic therapy "because it is available, inexpensive, safe and usually painlessly administered," they caution that it "can prolong the lives of many chronically ill patients."[6]

Wanzer et al. maintain, "it is morally justifiable to withhold antibiotics and artificial nutrition and hydration. . ." from patients in a persistent vegetative state.In their discussion of severely and irreversibly demented patients they state, "it is ethically appropriate not to treat intercurrent illness except with measures required for comfort (e.g. antibiotictcs for pneumonia can be withheld)." They distinguish these patients carefully from the "pleasantly senile" patient, who, depending on his or her prior wishes, may be resuscitated or placed in an intensive care unit.3(p.95)

The President's Commission report, addressing the question of the extraordinary status of antibiotics raised by Brown and Thompson, finds "there is no basis for holding that whether a treatment is common or unusual, or whether it is simple or complex, is in itself significant to a moral analysis of whether the treatment is warranted or obligatory.... If the ordinary/extraordinary distinction is understood in terms of the usefulness and burdensomeness of a particular therapy, however, the distinction does have moral significance. When a treatment is deemed extraordinary because it is too burdensome for a particular patient, the individual (or a surrogate) may appropriately decide not to undertake it."7 (pp. 87-8) Thus they conclude that there are "no particular treatments-- including such "ordinary" hospital interventions as... antibiotics--[that are] universally warranted and thus obligatory for a patient to accept. Neverthless, a decision to forego [sic] particular life-sustaining treatments is not ground to withdraw all care...(p. 90)."

Levenson reports a program to individualize treatment of critically and terminally ill residents of a geriatric center.8 There the Massachusetts General Hospital's levels of care are modified so that the third level of care,"limited therapeutic measures" includes the instruction, "Antibiotics should be used sparingly." Category four, "No therapeutic effort specifies:

> Only that which enhances comfort and minimizes pain.
>
> No x-ray examinations, blood tests, antibiotics.
>
> IV's ought not be started unless they will enhance comfort or minimize pain (p. 564).

This policy accords with that of the National Hospice Organization. In general, it is recommended that urinary tract infections and decubitus ulcers be treated with antibiotics and pneumonia be treated when the symptoms are distressing to the patient.[9]

Other Countries

There is no literature to suggest that other countries have limited the use of antibiotics for any group of patients or for any medical circumstance. Despite limitation in the use of expensive, high technology therapy such as hemodialysis, the United Kingdom does not limit antibiotic therapy.[10] The physician may exercise his or her discretion.

In Canada the proposed Canadian law reform would give the physician a legally protected discretionary power to act in the patient's best interest.[11] To date this reform has not been adopted. US commentators have observed that, although it offers physicians protection for the exercise of their discretion in matters such as withholding extraordinary treatment or therapy that prolongs dying, the proposed reform relies too little on the patient's wishes in making this determination.[12]

The Parliamentary Assembly of the Council of Europe in its Recommendation "on the rights of the sick and dying" declared that "the prolongation of life should not in itself constitute the exclusive aim of medical practice,which must be concerned equally with the relief of suffering." National commissions of enquiry were recommended "to determine the guiding principles for the application of extraordinary measures to prolong life," but the report did not specify these measures.[13]

Guidelines established by the Swiss Academy of Medical Sciences state that "If a possibility of improvement exists in a patient in danger of death from his illness or injury, the physician will take all measures necessary to heal and alleviate the condition." But "for a dying, a fatally ill or injured patient--whose illness progresses irreversibly towards death and --who will never be able to return to a conscious life involving human contacts, the physician alleviates suffering but he is not obliged to use all the therapeutic resources available for prolonging life.[14] Treatment that may be withdrawn or withheld includes medication as well as technical measures.

Summary

Antibiotic treatment is not customarily included in discussions of heroic or extraordinary measures because the professional standard of care is the routine administration of antibiotics for infection. Nevertheless, the Critical Care Committee of the Massachusetts General Hospital,[2] the policy of the National Hospice Organization,[9] Wanzer and his colleagues,[3] and the President's Commission[7] maintain that when antibiotics prolong the process of dying they should not be administered if they or the tests they require increase discomfort rather than relieving it. Brown and Thompson[6] and Hilfiker[4] suggest that this is current practice in the United States. In the mid-1980's, economic pressures, such as locally limited resources or space constraints, may tend to restrain the administration of antibiotics to elderly patients, especially when treatment involves transfer to hospital, complicated diagnostic procedures, and the consensus of family members upon whom the old person is dependent. A national consensus is needed to rationalize this variability of treatment, insuring that the outcome is consistent with the patient's wishes, and preventing both the under-treatment and the over-treatment of the elderly.

CASE 1 - THE COMMUNITY-RESIDING PERSON WITH A REVERSIBLE ILLNESS

Mr. B is a 73-year-old man who has been living independently in the community with the help of a daughter who brings groceries and helps out with chores and housecleaning. Mr. B's wife died 6 years ago of cancer after a prolonged course of surgery, chemotherapy, and radiation, and afterward he discussed with his daugher his desire for a "natural" death with dignity. At the suggestion of his minister he made out a Living Will.

Mr. B has cataracts which make driving difficult, congestive heart failure, and chronic obstructive pulmonary disease. With medication and medical supervision, his condition has remained stable for several years. Recently he began to cough up thick sputum, noticed dyspnea (increased shortness of breath) and pedal edema (swelling in his ankles). Mr. B paid a visit to his doctor, and oral antibiotics were prescribed.

After 5 days the symptoms persisted, and indeed, may have worsened. When his daughter became alarmed after a late-night visit, she phoned the doctor who recommended immediate admission to the local hospital where further diagnostic tests and treatment with intravenous antibiotics could be undertaken. Mr. B protested and despite his weakened condition made it very clear he felt near death and wished no further efforts or heroics be initiated on his behalf. His daughter and doctor attempted to reassure Mr.

B. that his chance for complete recovery was quite good and with treatment he would almost certainly return to his pre-morbid level of functioning.

Mr. B was admitted to the hospital: x-rays, blood tests, and other diagnostic procedures were completed, and oxygen therapy and intravenous antibiotics were begun. After 7 days of treatment, Mr. B began to improve, his mood brightened, and he began to enjoy food and fluids again. Several of his friends and neighbors visited him, and he enjoyed many cards and flowers from fellow churchgoers.

He privately has thanked both his daughter and his doctor for undertaking aggressive treatment on his behalf (despite his stated wishes to the contrary) and looks forward to discharge from the hospital and return to his home.

DISCUSSION

The Wishes of a Competent Patient

A competent patient has a right to change his mind even in the presence of advance directives; indeed, a competent patient's wishes always override his or her advance directives. Likewise, the physician is obligated to subject both those wishes and the interpretation of an advance directive to careful scrutiny in the light of what is known about the patient's competence, his or her disease and its prognosis. Mr. B. was a competent patient whose understanding of his condition and its prognosis were obscured for a time by his fear and, perhaps, depression. His physician and his daughter were right to procede with treatment. Advance directives, like the patient's immediate wishes, must be carefully interpreted and do not authorize poor medical care. Antibiotic therapy for Mr. B. was ordinary treatment.

It is not the case that a surrogate's wishes overrode the patient's in this instance. Mr. B's daughter is not a true surrogate because her father was never truly incompetent. But family members are important in reassuring and supporting elderly people who are ill and depressed. Both the daughter and the physician serve as support for the patient, educating him about the nature of his illness and encouraging him toward recovery. Both must be aware that depression may affect an elderly patient's will to live.[15] The role of physician is not altered by advance declarations; it remains to "do what doctor's do" : take care of patients.

Underlying condition

Mr. B's underlying condition, although serious, was stable. He was not dying, and there was every expectation that he could return to his previous level of function. The Living WIll, by its own terms, would not apply unless he was suffering from a condition that was irreversible and terminal, and therefore did not apply to his current situation. Had Mr. B.

been dying, the case would have been entirely different: if either the daughter or the physician been reluctant to withhold treatment when that treatment would seem to be prolonging an irreversible condition, the services of a social worker or a standing ethics committee would have been needed to negotiate their differences with Mr. B.'s advance directive.

Setting

Mr. B's care took place first at home and then in a hospital. The mission of the hospital is to provide acute care, including sophisticated tests, high-technological therapy, intensive care, and resuscitation The nature of their mission is reflected in their documented policies. This was the appropriate place for Mr. B. Had he been a nursing home resident, transfer to an acute care hospital would have been the treatment of choice.

Cost

Although an extraordinary amount of money is spent on patients in their last six months of life,[16] it is not possible to predict, except in a few well defined diseases, precisely when those last six months begin. Bayer et al. have concluded that there is no evidence that our treatment policies for the terminally ill are inequitable or unjust.[17] For a patient like Mr. B., then, who is independent and not terminally ill, there should be no question of unwarranted cost in connection with his treatment.

Extraordinary treatment

The few discussions of antibiotic use as potentially extraordinary treatment.[2,3,4,7,9] accord it that label only in the presence of terminal illness, a persistent vegetative state, or severe and irreversible dementia --none of which applies to Mr. B. Antibiotic treatment in his case was thoroughly ordinary treatment.

CASE 2: THE TERMINALLY ILL, HOSPITALIZED PATIENT

Mrs. W is a 67-year-old housewife. She lives with her sister, Mrs. J in a senior citizens' high-rise apartment complex. Both are widows and neither has had children. They have enjoyed each other's compaionship for the past 7 years. Mrs. W. underwent a radical mastectomy (removal of a breast and underlying muscle) approximately 1 year ago. At that time malignant cells were found in the breast tissue and the lymph glands, which indicated that the cancer had metastasized beyond the primary site in the breast. Further surgery was ruled out; however, radiation and chemotherapy were undertaken when Mrs. W's condition permitted. Despite the poor prognosis and after discussion with her doctor, Mrs. W agreed to this. But she did not tolerate the radiation and chemotherapy very well and she has suffered much nausea, vomiting and pain during the past 6 months. Her sister, herself in her 70's, has attempted to care for her at home, but the constant demands of Mrs. W's condition have drained Mrs. J of physical and financial resources.

When Mrs. W developed shortness of breath and difficulty breathing, Mrs. J become highly anxious, phoned the ambulance and demanded that Mrs. W be admitted to the hospital, as she could not cope with the additional care demands imposed with the new symptoms. On admission

Mrs. W was found to have a temperature of 102.8° F with an increased pulse (96 per minute) and respirations (34 per minute) and, on ascultation, numerous rales (crackles) were heard throughout the chest. X-rays confirmed pneumonia and numerous cancerous lesions in both lungs. Mrs. W became comatose, was intubated and treated with antibiotics for the pneumonia and admitted to the ICU. Her fever gradually resolved and the pneumonia symptoms improved. However, several attempts to wean her from the respirator proved unsuccessful. The pneumonia, the effects of cancer, and her general weakened condtion had precipitated complete respiratory failure.

Mrs. J asked that the respirator be removed and antibiotic treatment discontinued. She stated her sister did not want to be a further burden to anyone, and the events of the last several months had broken her spirit and will to live. Mrs. W's physician noted in the chart that her condition was terminal and should she survive the pneumonia, she would probably die within 3 months from the cancer with continued pain and discomfort. Therefore, at 2:30 P.M., on the tenth day after her admission to the hospital, Mrs. W's respirator was disconnected and 15 minutes later, Mrs. W died quietly secondary to respiratory arrest. Mrs. J was unable to be present at her sister's death and wished only to be informed by the doctor when the death had occurred and the ordeal was completed. She explained her mental and physical exhaustion had rendered her unable to cope with her sister's illness, suffering and death, despite the close relationship they had enjoyed for the past several years.

DISCUSSION

When a patient lacks decision-making capacity, the treatment process becomes complicated and cumbersome. Some interventions that are customary (or even obligatory) for nonterminal patients may become optional or sometimes frankly contraindicated in the case of a dying individual. Despite Mrs. W's failure to communicate an advanced directive regarding her treatment preferences to her physician in the event she should become incompetent, her life pattern suggests that she would opt for aggressive therapy. She had, after all, agreed to anticancer treatment which caused her considerable physical and emotional discomfort. Therefore, despite her terminal condition (less than three months to live,[8] the outcome of this case may be questioned.

The traditional professional liability or malpractice principles impose upon the physician standards regarding quality of care that are fully applicable to older patients. The fiduciary or trust relationship between physician and patient requires that the physican act always with the patient's "best interests" in mind.[13, 5] Regardless of the setting, for the competent patient autonomy and self-determination prevail, and based upon information and recommendations from the physician, the patient either accepts or refuses antibiotic therapy. It is recognized that competent patients have the right to refuse treatment, even if their refusal would make death inevitable.[7] (The treatment of competent patients against their will is considered to be assault, and under these circumstances, the physician's obligation is construed to include provision of information to the patient to fully apprise him or her of the treatment options and their consequences.[19]

However, in Mrs. W's case she was unconscious and thus incompetent to participate in decisions regarding her care. Mrs. J was the only living relative and her sister's proxy decision-maker when she became incapable of participating in decision-making. In the absence of advance directives to the physician, family members or significant others often provide indications of the patient's wishes. However, Mrs. J does not meets the criteria advanced by Pellegrino and Thomasma necessary for the proxy to be considered a valid representative. These conditions include: the competence of the proxy, a known relationship to the patient and the ability to represent the patient's wishes, and a concern for the patient's welfare unimpaired by a conflict of interest.[20] In New York state, however, Storar established that family may not give substituted judgment as a proxy decisionmakers for persons who have never formulated their wishes or have not previously indicated those wishes. (In Conroy the patient had been judicially declared incompetent and her nephew was a court-appointed guardian of her person. In Quinlan, the father was a court-appointed guardian.) In Mrs. W.'s case, the sister is giving substituted judgment without legal status to do so, and clearly her own interests are directly involved. Many physicians are aware of these potential conflicts of interest when family members undertake decision-making for impaired relatives. (See Appendix II A, Phyisican Interview p15). Mrs. J stated that her sister said she did not want to be a burden to anyone; however, that cannot be translated to mean she did not want to live.

One can only wonder if this hospital had a documented policy stating criteria necessary for the removal of life support machinery and termination of treatment. If so, it might have called for the examination of the patient by two independent physicians to verify the terminal condition, the approval of the ethics or treatment preference committee, involvement of an ombudsman, or other safeguards. (See Appendix II B, Monroe Community Hospital Guidelines).

The cost of illness, especially care of the dying, has been raised as a criticism of the health care system.[5] Detsky and colleagues concluded that criteria for admission to intensive care units were crucial to cost containment.[16] However, Bayer et al. maintain that despite heavy expenditures during the last months of life, there is no conclusive evidence that our social policy of treating the terminally ill is disproportionate, unreasonable, or an unjust allocation of societal resources. They concur with the need for better cirteria for ICU admission and recommend "promotion of patient and family autonomy with regard to decisions to stop or refuse certain kinds of treatment; and promotion of alternative forms of institutional care, such as hospice care."[17] Kapp maintains that the President's Commission conclusion "that society has an ethical obligation to ensure equitable access to health care for all... is in no way modified by the age of the person in need of treatment."[5] By not undertaking aggressive treatment for Mrs. W. (intubation, treatment with antibiotics), the physician may have not been meeting the criteria of standard medical practice and thus may have left himself open to potential criminal liability and licensure problems.[21]

Nevertheless, treatment once regarded as routine increasingly may be withheld--or even withdrawn--if it is invasive and serves only to prolong dying. One wonders if Mrs. J and Mrs. W would have been better served by enrolling in a hospice program. Programs of this sort provide home services and respite care to relieve primary care providers, thus preventing exhaustion and burnout in these care providers.[22] Also encumbent in hospice programs is the discussion with patients and families of their treatment preferences in advance of crisis, with an emphasis on palliative care, so that if Mrs. W had agreed to participation in a hospice program, she would never have been admitted to an ICU.

The role and responsibility of caregivers involved in the decision to administer or withold antibiotics in the case of critically ill or dying elderly patients ranges from the specialists, who are appropriately aggressive in the recommendations, through the attending physicians, who have the responsibility for the decision to the nursing staff, who implement decisions and work intimately with their consequences. House staff, still in the process of learning clinical care, have a legitimate interest in the specialist's recommendations but this may blind them to the personal context of the illness or the social context of the decision. Yet, on the other hand, they are responsible for patient care without the authority or, often, the necessary information and support to make decisions.[22] Dr. Hilfiker notes in response to Dr. Lebel and his colleagues that he is worried because residents seem to be receiving so little preparation for the difficult role that awaits them as practicing physicians.

CASE 3: THE NURSING HOME PATIENT IN A CHRONIC VEGETATIVE STATE

Mrs. G. is a 92 year-old widow who was admitted to a Skilled Nursing Facility 15 years ago. Dr. Smith has been her attending physician for the past 25 years. Initially, she required daily care because of her failing eyesight and early signs of Alzheimer"s Disease, but now she is blind, suffers from advanced Alzheimer's Disease and is confined to bed. She is fed by a nasogastric (NG) tube (nose to stomach), is incontinent of urine and feces, and is contracted in a fetal position. Occasionally her movements suggest to the nurses that she may be aware of the activities around her. Her only living relative is a 69-year-old niece who lives nearby but never visits.

Her stay in the nursing home has been complicated by repeated urinary tract infections (UTI's) that were initially cultured and treated as had been Dr. Smith's practice in his office. The increasing urine (and fecal) incontinence, however, has required an insertion of a chronic indwelling bladder catheter to avoid serious breakdown of the skin covering her sacrum (posterior lower back). With the indwelling catheter in place, antibiotics would no longer clear the UTI's and the bacteria in the urine were now resistant to all but a few of the most powerful and toxic drugs. Now, whenever she developed a fever, the nurses provided extra fluids and the temperature gradually returned to normal. Recently, however, Mrs. G. has developed a pressure sore (decubitus ulcer or bed sore) that has not responded to conservative therapy.

One evening when turning Mrs. G., the nurses notice that she feels warm and cries out in apparent pain. Her rectal temperature is 104° F and she is having difficulty breathing due to thick secretions accumulating in her throat. Oxygen is started to help her breathing, but she is agitated and pulls out the nasal cannula. While restraining her arms, the nurses further notice that the sacral pressure sore is draining foul-smelling prurulent material and there is an area of redness beginning to form around the ulcer. Mrs. G's restlessness continues and the nurses note her discomfort and notify Dr. Smith.

Unfortunately, Dr. Smith is out of town but his junior partner, Dr. Jones is covering. Dr. Jones is unfamiliar with the patient and would like to order a chest x-ray and a sputum culture to rule out pneumonia. He is aware that she has had chronic UTI's associated with the indwelling bladder catheter and knows that blood and urine cultures should also be ordered. He is also concerned that the septicemic-like picture could be due to the pressure sore with possible underlying osteomylelitis which probably would require surgical debridement. All of these studies and the appropriate treatments require transfer to the acute hospital. The nurses notify Mrs. G's niece who responds, "Don't bother me with her problems. I've got problems of my own, and I never cared much for her anyway."

When Dr. Jones visits and assesses Mrs. G he notes her contractures, her high degree of restlessness, and her apparent discomfort. As he feared, the physical examination indicates that one or more of the infections that he considered on the drive over, are very likely. She looks as if she is septicemic due to the infected pressure sore, and her condition is rapidly deteriorating.

Dr. Jones is unsure how to proceed. Mrs. G. has left no advance directives regarding her treatment preferences and Dr. Smith has left no notation on her chart to indicate her care preferences in the event of a life-threatening infection. The nurses verify that Dr. Smith has never discussed treatment preferences with the niece, but express concern about the transfer to a hospital which will cause Mrs. G further discomfort and amplify her restlessness. Despite the fact that Mrs. G's chances for recovery even if treated are uncertain, Dr. Jones decides he must treat these intercurrent and potentially reversible infections aggressively, and he transfers Mrs G to the nearby University Hospital.

Her first 6 hours in the hospital consist of two complete physical examinations by the intern and the resident, x-rays of the sacrum and chest to rule out pneumonia and osteomyelitis. Multiple laboratory studies (blood counts and blood chemistries, urinalysis, and cultures of the blood, pressure sore, and urine) are also undertaken. Mrs. G is restrained during the multiple venipunctures. Because she is unable to cough up sputum, a nasopharyngeal aspirate (requiring the insertion of a small plastic tube through the nostril down to the back of the throat) is performed. This causes Mrs. G to gag and vomit, choking and aspirating some vomit into her lungs.

The tests reveal pneumonia, an active urinary tract infection, but no osteomyelitis. The culture results will not be available for several days. Because of the evidence of three major sites of infection and probably bacteremia, the house staff wants to treat Mrs. G with three intravenous antibiotics: ampicillin, gentamycin, and clindamycin. Dr. Jones would have preferred a regimen with less toxicity, but agrees that the drugs' coverage is excellent and, after all, realizes that he himself has initiated her transfer to the hospital. A general surgeon also sees Mrs. G and arranges for her pressure sore to be debrided in the operating room to prevent complications from osteomyelitis.

The last week of Mrs. G's life was stressful for her and her care providers. Although she initially improved, she rapidly developed pulmonary edema (fluid in the lungs) as a result of all the intravenous fluids that were required to deliver the antibiotics. This was aggressively treated with intravenous diuretics and digitalis which lowered her serum sodium and seemed to increase her restlessness. During the night, the restraints loosened, and Mrs. G fell out of bed and sustained a fractured hip. As she had been confined to bed, it was decided not to repair the fracture surgically. On the 7th day, the fever returned, Mrs. G became more short of breath and very restless. A repeat chest x-ray demonstrated a rapidly progresive pneumonia in the right lung. A second nasopharyngeal aspirate was performed and demonstrated white cells and what appeared to be a yeast infection. Because her kidney function was progressively deteriorating (probably from the combination of drugs administered in the hospital), it was decided not to treat the pneumonia with further antibiotics. She died 3 days later with progressive pneumonia and renal failure. The nurses and doctors involved in Mrs. G's care seemed relieved that her suffering had finally ended. A memorial service was held in the Nursing Home where she had resided for 15 years, but Mrs. G's niece chose not to attend.

DISCUSSION

Hilfiker[4] has described the physician's dilemma when treatment with medicine at all stages of illness is standard medical practice in the community, but the caring physician somehow judges that medical intervention would be proonging the process of dying rather than extending life. The flood of thoughtful letters in response to Hilfiker's article suggests that he touched an exposed nerve in the medical community. None of the respondents advocated full treatment. They differed only on the issue of where physicans should seek guidance in such decision making. The majority of respondencts regarded such decisions to withhold treatment as the essence of the "art of medicine." In his reply to the correspondence, Dr. Hilfiker focusses the medical dilemma more precisely: his patient, although irreversibly cognitively and physically impaired, was clearly a live, sentient human being, indeed, a "person" who occasionally smiled and laughed. Like Schneiderman and Arras in their essay on physicians and advance directives,[23] he urges the medical profession to explore the problem within its ranks and to communicate with their patients so that a societal consensus might emerge. He expresses fear that in the absence of such an evolution of societal values, guidelines may be imposed by courts and governmental entities on what should be a physician-patient decision.

Brown and Thompson[6] studied the use of antibiotics in nursing homes. They identified a pattern of nontreatment that correlated with several factors: the patient's diagnosis, mobility, pain, sudden deterioration, the size of the facility, the number of narcotics prescribed, and physician's relationship with the patient. Significantly, there was no correlation of non-treatment with dementia. Too, physicians who had no long-standing relationship to the patients as whole persons were the most likely to treat. Responses to the article criticize the authors' failure to indicate the patients' treatment preferences or, indeed, clear evidence that these preferences were consulted.

The lack of advance directives in the form of a personal communication to the physician, a Living Will, the designation of a durable power of attroney, or an appropriate surrogate family member combined with the patient's compromised competence and an unfamiliar covering physician, resulted in an unsatisfactory resolution of Mrs. G's medical problems. The divisions in interests and respnsibilities among the patient, the family (if present), and all caregivers--to say nothing of individual attitudes and beliefs--produce tension and variability in the decision-making process and in the outcome.[24,25] In some cases, this may result in lack of aggressive diagnosis and treatment, and in other cases, like Mrs. G's, overtreatment may result.

With patients like Mrs. G who possess a poor quality of life, the caregivers either explicitly or implicity consider this factor when arriving at medical decisions.[26] However, it has been illustrated that physicians' perceptions of a patient's quality of life demonstrate marked variability. Pearlman and Jonsen noted that consideration of quality of life was associated significantly with several factors including the patient's prior medical experience, the amount of supplementary case information, estimates of the patient's survival time, and attitudes about medical responsibilities/patient rights.[27] As many of these factors are highly subjective, the resultant variability is not surprising. Wolff et al.[28] have demonstrated a contrast between the actual treatment practices undertaken in a 200-bed voluntary, nonprofit nursing home and nurses' perceptions of appropriate treatment based upon assessment of the patient's quality of life. They note that physicians continue to presume in favor of more intensive treatment and that families, subsequently, concur in such a presumption. Nurses in the same circumstances prefer conservative intervention when the primary patient characteristics include immobility and unresponsiveness. Nurses also tend to acquiesce in depressed patients' requests for non-treatment in an apparent desire to prevent the individual suffering which might result from hospital transfer and aggressive treatment. In a supplementary study by Tabloski psychosocial factors in the elderly are examined for their correlation with antibiotic treatment decisions.[29] These findings will be forwarded in the near future. All these secondary judgments may be hazardous and may seriously underestimate the patient's own perception of life's worth even when that life entails suffering.[30]

In Mrs. G's case, the nurses prefered that Mrs. G not be transferred to the hospital as they felt that this would cause her further discomfort while offering little hope for recovery; Dr. Jones, new to the case, opted for standard treatment. Lack of communication among members of the health care team adversely affects treatment decisions.[31] Management rounds, particularly for patients who have no family, have been proposed as one solution.[32]

Within the nursing home setting, antibiotic treatment decisions often involve the transfer to an acute-care hospital, the insertion of an intravenous line, multiple injections and venipunctures, and the application of restraints to discourage removal of monitors and tubing. In addition, the untoward toxic effects of antibiotics are well known; they range from rashes to severe diarrhea, nephrotoxicity, bleeding disorders and death.[33] In Mrs. G's case, she suffered nephrotoxicity which limited further treatment and eventually lead to her death. Her care was further complicated by her broken hip, resulting from a fall from bed, itself a consequence of increased agitation; both are documented as too-frequent outcomes of acute care hospitalization experiences of the frail elderly.[34] In addition, the suctioning of sputum from Mrs. G's throat (nasopharyngeal aspiration) caused her to vomit and inhale her vomitus, further complicating her pneumonia. Some authors advocate the establishment of lower-tech hospitals or higher-tech nursing homes which can provide intravenous therapy by which to deliver antibiotics to the frail elderly and thus provide aggressive treatment within a familar setting to eliminate some of the risks of hospitalization.[28]

When undertaking a course of treatment for an individual incompetent patient without advance directives, the decision-makers should undertake an analysis of the benefits/burden ratio for the patient.[35] Lynn notes that for most people at most times, the prolongation of life is a very important objective. Outcomes frequently include cure, relief or prevention of disablitity, comfort and cymptom control, enhanced capacity for human relationships, restoration of competence and control, the opportunity to eomplete important tasks, amelioration of detrimental effects on loved ones, and delay of death.[36] However, sometimes the conditions that are necessary in order to prolong life are too burdensome to the patient for the endeavor to be worthwhile. Whereas antibiotics are usually considered a rather common and minor intervention (with low burden and high benefit), the administration of these antibiotics may entail transfer to a hospital, intravenous lines, and application of arm restraints, which constitute a high burden When the treatment becomes too burdensome in itself, it may actually promote sufering and cause distressing secondary symptoms as it did in Mrs. G's case, where as a result of the hospitalization and antibiotic therapy she went into congestive heart failure and renal failure with restlessness and discomfort. It was only then that Dr. Jones decided to terminate further antibiotic therapy and provide comfort care only.

Legislatures have consistently failed in the Natural Death Statutes to include medicines, including antibiotics, in the definitions of "extraordinary" treatments. However, prior to Delaware's passing a Natural Death Statute, when confronted with the detailed medical facts, the Severns court[37] clearly and unequivocally concluded that in that particular case antibiotic treatment was a heroic measure which need not have been undertaken. (See Appendix II-C for a detailed discussion of Natural Death Statutes and and the Severns case.)

The definition of what constitutes ordinary or extraordinary care and how this relates to criminal liability needs clarification. Doctors are fearful of a too restrictive definition, disallowing some discretionary space.[30] In Mrs. G's case, Dr. Jones was concerned that the combination of ampicillin, gentamycin and clindamycin might be too toxic, but declined to alter the order, noting that this was the treatment of choice within that institution and that he, after all, had initiated the transfer. In other words, this aggressive treatment protocol was ordinarily undertaken in this institution and to do otherwise would have been somehow extraordinary.

Decisions about treatment for seriously ill incompetent patients are increasingly regarded as not a matter for the courts to decide.[38] For the formerly competent patient, exemplifed by Karen Ann Quinlan and Brother Fox, the emerging consensus is that the patient's wishes expressed when competent are to be sought to provide a guide for present action. Lacking advance directives, as in Mrs. G's case, substituted judgment may be constructed from the patient's life pattern.[39,22] For this purpose family members and friends provide important clues.[40] Mrs. G's niece, her only relative, was contacted but refused to become involved in the treatment decision. As this case had to be quickly decided in the middle of the night, Dr. Jones decided to treat Mrs. G aggressively. He may have based his decision upon the following factors: The patient has a potentially reversible disease and is not "terminal"; she has no advance directives or designated proxy, and therefore traditional medical responsibility mandates the physician act in the patient's "best interests."[21] Mrs. G has been a patient of Dr. Smith's for 25 years, and presumably has been ill with infections during that period and is still alive; therefore it may be assumed that she chose aggressive therapy in the past in order to have survived until the present time. However, when the infection became overwhelming and the patient was compromised by over-treatment, no further therapy was undertaken. The best interest argument can then be construed to withdraw further aggressive antibiotic treatment as these treatments can not prolong life, but are rather prolonging the process of dying.[5]

Implicit in any discussion of limiting treatment is the expectation that the patient's suffering and distress will continue to be sensitively assessed and that palliative treatment will be provided for the relief of distressing physical symptoms and pain.[26] The patient is not abandoned by the medical and nursing staff. Besdine further notes that despite sensible decisions to limit treatment, the comfort of the patient may demand specific therapeutic interventions for an unexpected, intolerably painful illness. Decisions not to treat can never be absolute, and assidious attention must be paid to comfort measures and relief of suffering. This is consistent with the mission of health care institutions, standards of professional licensure and practice,[21] and the role and ideals of the health care professions. To undertake to ration expenditure for beneficial medical care on an individual basis is "inconsistent with [medicine's] role as advocates for the health of our patients."[41]

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APPENDIX II-A

Background Statement for the Interviews: The Office of Technology and Assessment which is part of the U.S. Congress system, is evaluating life-sustaining measures for the elderly including resuscitation, ventilation, hemodialysis, nutrition and fluids and antibiotics. We have the contract for antibiotics: They want to know if an older person has a life-threatening infection which requires to make a decision to treat or not to treat. By life-threatening I mean that if not treated the patient will probably die of the infection within a couple of days of onset. The OTA are interested in learning what are the antibiotic treatment practices with elderly people and

Wheras We have experience in this area it's very specific and related to Monroe Community Hospital. We want to talk to a number of people who represent the broad fields of medicine who care for older people. We are trying to find out how do you decide to treat or to not treat an older person and does the process differ in terms of the setting that you're in. Would it differ if you had a patient that was in the community and came to you with a life-threatening infection in the office or you saw him in the emergency room, etc., versus if you saw them in a nursing home versus if you saw them in a hospice-type setting. Would a particular infection influence your decision to treat or not to treat. The specific life-threatening infections that we have selected are pneumonia, urinary tract infection with septicemia, pressure ulcer with spreading cellulitis and suspected septicemia and as an example of an iatrogenic infection, septicemia associated with indwelling venous catheters used for total parenteral nutrition.

There are no right or wrong answers here. Based on experiences here in Rochester we will try to give OTA some insight into how physicians make these decisions. We think that the people that we talked with will be very representative of what-------- physicians around the country. Do these specific infections differ in terms of in terms of how much pain or discomfort the patient experiences, i.e., the burdens placed on patients with this type of infection. These are probably issues you wrestle with every day. Finally, we would like to focus on two medical conditions that older persons frequently are faced with. One would be the terminally ill person who would be a person destined to die within 6 months regardless of what you were going to do. In other words thev have an underlying disease that is incurable regardless of whether you can cure the infection. The the other condition the elderly patient is critically ill, i.e., the person has a life-threatening infection but their underlying disease(s) are not going to kill them within a definate relatively short period of time.

1. Edited Transcript of Interview with 63 year-old Physician in the Private Practice of Internal Medicine:

Interviewer: In general terms, what would you say are the steps that are involved when you make decisions to treat or not to treat?

Physician: Certainly, in my thinking of most therapy, including antibiotics, I am trying to think of what are my goals for the patient and am I, in my treatment, helping the patient to survive and to live or has the patient reached a stage in aging and illness, where I am really thinking of my goal as helping the patient to die comfortably. I may shift gears as my goals change for that patient. The point at which I shift gears is rarely easily arrived at. Let's take, for a moment, the patient in a nursing home. Some of them are there and st are in good sound mind, or reasonably sound mind, and enjoy participating in activities and the quality of life is such that both they and the family and I would feel that is quite appropriate to be aggressive in therapy, and all that we do, including antibiotics. If they have pneumonia or a life-threatening infection I would treat with the same intensity that I would treat a younger person.

At the other end of the spectrum, would be the patient who has metastastic CA. Here they are not going to die within the next week probably, but in a matter of a few weeks or months. During those weeks and months they are going to be in discomfort and pain, and part of the battle will be in pain medication, which often produce side effects. At this point in the downward path, if a person got pneumonia, I would have to think seriously whether I wanted to treat it at all. Would I be doing the patient a favor to let the pneumonia take that patient then rather than picturing a number of weeks and months of pain and discomfort and a declining quality of life. So that the decision in that patient, as with all instances, would be based upon one's knowledge of the patient's wishes and the patient's participation in decision-making in so far as that patient mentally is capable. My discussions with the family would be in a positive way; namely that I would recommend not treating the patient because I think it will merely prolong the act of dying and cause more suffering. Not asking the family do you wish me to give the antibiotics or not because that can be setting the stage for guilt in future times for them. Rather saying this is what I think we ought to do. Usually an agreement is made but then they can assign me that responsibility.

Interviewer: Those are two extremes; there are certainly a number of situations where the downward course is a progressive one but there is no cancer that gives you some feeling for prognosis.

Physician: And this may make up the majority of patients in nursing homes who just have the dwindles, are in their 80's or 90's, and have varying degrees of mental capabilities. Some of them are totally beyond talking or entering into any decision-making or understanding anything. In these patients I am always having ambivalence within me but my sympathies are with helping these patients to die rather than prolonging what I consider a suspended sort of life that has lost its meaning and purpose. In that situation my goal is for comfort and not to very aggressive in prolonging that meaningless life. I may very well not treat. There are some situations where family wish treatment of all their varying needs. I have a women like this at the moment who is in a nursing home and bilateral kidney stones. She is in her late 70's and she keeps getting recurrent infections with increasingly more resistant organisms as one treats several infections over the years. I have talked to her son about optio about bringing her into the hospital and removing the stones, treating each one as it comes along or treating symptomatically with tylenol. It often happens that there is a fever spike and then she goes along for weeks with no fever. We simply stopped treating as the infection is resistant to most antibiotics. Her son elected not to have surgery so we are treating symptomatically. So far, she has not gone into gram negative sepsis and died but she may with one of these episode

Interviewer: So you're speaking with a valid representative, her only s Has he been designated by her in some formal way or is it just...

Physician: He had power of attorney and he is very interested in her.

He is an engineer. I took care of her husband, I know the family an clearly he is the right one. He is legally responsible as her nearest relative but also he has always been responsible, as she has gone down hill, for her affairs and she has accepted it.

Interviewer: So now you are at your this point of discussion with him that if she did become septicemic and...

Physician: He would not want me to treat it.

Interviewer: In that particular case of pylonephritis or obstructive urinary tract infections is that kind of infection any different, in your mind, in terms of causing discomfort to a person than lets say a pneumoni Is this particular infection a difficult infection to a more difficult infection to withold antibiotics than say pneumonia would be or about the same because you can treat the symptoms? In a...

Physician: Your point is well taken as my concern for some of these people is mainly their comfort. I've lost interest in trying desperately to prolong their life when it has become meaningless but I am interested in their comfort. That is the one major goal; that I help them die comfortably. In my own philosophical approach to that I am willing to us treatment to make them comfortable which may prolong their life just as I am willing to give treatment for comfort that might shorten their life. In pain medication, morphine might conceivably shorten someones life if it makes them comfortable. It is true that antibiotics given to reliev some symptoms might possibly prolong life. If comfort is the primary goa than one has to accept the spin off whether it shortens or prolongs. If a patient in the nursing home setting is having a lot of dysuria and a lot of discomfort, certainly treatment of the urinary tract infection, not necessarily life-threatening, would make sense. And even life-threat might make sense. If there is a _____ asymptomatic infection, I may choose not to treat. Fever can be controlled but you never know what they are going to do on their own and, in this patient, she is going through now a number of episodes of fever for a day or two dropping off to normal and going on with minimum discomfort according to my estimation and the nurses and is simply not treated. So I don't know. I'm not sure that I would say that where the infection is in the body makes much difference but the amount of discomfort it might cause.

Interviewer: In your experience, if we look at those four infections or lets say the first three, do they seem to be any different in terms of the amount of discomfort that they cause e.g., pneumonia, urinary tract infection, usually pylonephritis, or at least an outflow obstructio problem at some level, and a pressure sore.

Physician: Pressure sores, I would think, are probably frequently uncomfortable and I treat those vigorously. But in the last ten years, I can only think of one patient who got into really serious difficulties. The nursing homes my patients are in have done a remarkable job in preventing these, better than they were 20 years ago," I think. I can think of one patient who was incontinent and got pressure sores, one of which was quite severe, required surgical ~~consult~~ for debriding and antibiotics and so on. I would feel most pressure sores are not life-threatening. In an acute situation they can be but they are more chronic discomfort in my opinion with a potential for life-threatening infection. I would treat these, in general, because it is an uncomfortable issue for them.

Interviewer: Do you see the pneumonia and urinary tract infection sepsis cases differently?

Physician: Well, I would see the pneumonia on a statistical basis more life-threatening than most decubiti which I have experienced in over the last 10 years although they can be very deep and necrotic.

Interviewer: How about from the discomfort point of view to the patient rather than the outcome?

Physician: Pneumonia of course varies a great deal and many of the patients quickly become relatively obtunded and I think of this as being on the whole spectrum. I can see pleurisy. I can see some patien who have a great deal of discomfort whereas others are simply obtunded or become comatose.

Interviewer: Is hypoxia or dyspnea a very uncomfortable phenomenon for the patient who has a life-threatening pneumonia?

Physician: I'm sure it is if they are alert. But here is a gray area where we are trying to decide what our appropriate action is. I suppose pneumonia would be one that I have not treated if I have reached a point of thinking of helping the patient die comfortably. I might be willing to since they have often become obtunded fairly early and died fairly quickl I may give them oxygen, and most nursing homes can do that now. If our decision is to help the patient die comfortably I have not used antibioti but rather let them die.

Interviewer: For the elderly patient who is in the community, competent and seeks help with a life-threatening infection, or for one you hospital immediately after talking with the family over the phone, is there any difference in how you manage these patients (in terms of this question of treatment or no treatment) versus a younger person.

Physician: If they are a functioning individual, enjoying life regardle of age, I don't treat them any differently. I approach them as people w high life-quality and we are obligated to help them.

Interviewer: Sometimes you see elderly patients with chronic pulmonary disease who are in and out of the hospital with recurrent episodes of pulmonary insufficiency. Here other issues arise, such as whether to intubate or not. Is this different from the choice of using antibiotics or not.

Physician: I think that becomes a tougher decision because the patients frequently, after some intubation, may not want it. But in general my approach to the functioning individual is all out help.

Interviewer: And whatever their wishes are is what you'll honor?

Physician: Yes. This assumes that the patients who are functional are anxious to continue to live. But it gets a little stickier in some of the border line pulmonary function patients who say, " I don't want to go back to the Unit. I don't want to be intubated again. Maybe it is o to use antibiotics but not intubation."

Interviewer: Does the fact that these patients are in the hospital for this care add any different pressure on you in terms of how you decide whether to treat or not treat with antibiotics? Secondly, how do you evaluate the question of depression, which may be very situational and i fact may be, in your experience, somewhat temporary? How do you deal wi the patient who may be depressed and says, "No, I don't want to do this." Yet, the patient is competant in terms of being able to engage in these types of decisions.

Physician: You're raising some very funny ----issues. There are two questions there. The first is the setting, whether community, nursing home or hospital. There are psychological pressures in a sense that a patient introduced into the hospital sort of gets fed into. The routin of the house staff and nursing staff are all geared primarily to use all methods possible to help patients, who may have already been started on antibiotics at the time they reach the hospital. Things can go fast and it is hard to stop something once you have started. But with patients with terminal CA, for example, I have found that the house staff and nurses, in general, are relieved if someone else makes the decision to withold certain treatment, to help patients die without agressive therapy. They have been thinking about it and wishing, but may not be willing, to take that responsibility. I suppose these are psychological pressures on all of us to use the weapons that are readily available in the hospital. In the nursing home, those weapons are not immediately available and there maybe just a little less pressure to do everything. It's a little easier; I don't have to wrestle with any other person. Although I have been impressed with how the staff is devoted to patients who have been there for years, who have varying degrees of personhood left. I have seen a number of nurses truly grieving the death of some patients with whom they had become very attached. The setting does affect the decision-making in an indirect sort of way. If ones goals are in trying to define the goals clearly, the setting doesn't make any difference but it just requires more people to deal with.

Interviewer: Before we go on to the second part, have you had any experience in managing life-threatening infections in patients in the hospice setting or in patients who are at home with the expressed purpose that that's where they are going to die? Does that setting affect how you decide to treat or not to treat?

Physician: I have used the formal hospice program in the last two years they have gone very well.

Physician: Well, by definition at that point the patient, family and physician have all agreed on the goals which are: 1) to help them die and 2) to face their approaching death comfortably. I haven't had to deal with a kidney infection or a bedsore. But I'm not sure that it would affect my decision-making. It would be based upon the person's mental competance, their ability to sense pain, to perhaps enjoy or need to survive for a given period to accomplish something.

Interviewer: In a nursing home setting you really cannot treat a life-threatening infection because it requires intravenous antibiotics and there is the added issue about transferring to the hospital in order to implement your decision. How does this affect your decision-making process?

Physician: It is one more step obviously that is required before the decision can be made. For some patients with pneumonia I have used antibiotics, penicillin, intramuscularly. This obviously is sort of a compromise in a way in that you're not doing quite as intensive therapy as you might.

Interviewer: Ordinarily would these cases have required hospitalization because they were life-threatening or were really moderate-to-severe pneumonias?

Physician: Pneumonias are always potentially life-threatening in the elderly patient. I certainly may decide to treat a pneumonia this way which is not too severe. On the other hand, I have transferred patients to the emergency room for chest x-rays, blood cultures, etc., if that is the patient wishes and we are going all out. Is this the same basis you use when seeing a patient in the office with pneumonia when you deci to treat as an outpatient or hospitalize?

Physician: I don't think there is a great deal of difference. Underlying all of these decision-making processes is the question; what our goals for the patient. For some nursing home patients certainly the goal is appropriate to go all out.

Interviewer: We left this other issue, depression. How does this interfere or complicate the situation?

Physician: I think it obviously complicates it. I guess one has to take into account the patient's past track record on bipolar mood swings and their status. Is the depressed mood a realistic one? Is it based on there grieving which is somewhat different from sheer depression? Certainly a person who is facing a death or loss of functio in any way may become quite depressed. If it seems that their depressio influences their desire not to take treatment or if their objection to treatment is based upon a perception of the facts that doesn't agree wit my understanding of their potential for recovery to a reasonable life quality I'm more likely to twist their arms, talk with the family and attempt to encourage them to take that which they don't want.

One does this frequently in patients facing decisions of chemothera for cancer for example. Chemotherapy is a dirty word to many patients; it's constant discomfort. One has to educate them as to what they are facing so that it's more likely to come up in that situation than it is with I think with decisions about antibiotics specifically. I just can't remember a depressed patient saying to me they didn't want to have antibiotics for pneumonia or urinary tract infection. Certainly, it might arise. If one is convinced that the patient is depressed one may certainly seek a psychiatric consult, may use antidepressant medication and do one's best to convince the patient that the treatment is in their best interests. Overall assessment of the realistic patient is realistically appraising what it is going to be and if you agree with them that life is be closing in very rapidly on them, even though it seems appropriate, one may not try to argue them out of it.

Interviewer: I understand how you have been approaching this and it see very rational to me but I wonder if this is very different for house sta You mentioned that you used your past knowledge of the patient etc. Have you noticed that when you share the responsibility of caring for the pat in the hospital setting whether the house staff have some different probl Have they worked this through the same way that you have giving the patie the ultimate control of the autonomy when they are competent to make thes decisions? Is this part of your teaching to the house staff? Are these dilemmas and proposed ----- discussed in the house staff training?

Physician: I'm not sure what contact the psychiatry liason service has the house staff at present. Certainly over the years I have seen the house staff run rather rough shad; doing what they think had to be done regardless. On the other hand, I have the utmost admiration for the sensitivity of many of our house staff. I think the medical/legal issues have been addressed in the forfront in recent years and, somewhere along the line, the house staff have been alerted to their ethical/legal respon bilites; There is nothing that I can think of in the last year or two tha was a major conflict of the house staff.

Interviewer: You mention ethical and legal responsibilities; what did yo mean by that?

Physician: We had last week a Grand Rounds on medical-legal issues of the care of the dying patient and decision-making responsibilities. I legal issues are still evolving. Some of them in directions that I am enthusiastic about: involving court appointed guardians and so on. Major cases that sometimes get dragged out into a complicated mess. The legal issues, such as who is responsible for the incompetent patien has undergone major changes in time. They do not always seem to me to coincide with the ethical issues: the responsibilities of doctors to carry out the patients wishes that have been expressed or be agreed upon in advance living wills, the responsibility of the famil and doing what you think the patient would want. Sometimes that confli with court decisions. I have not been involved personally with any committee or persons appointed for representation. There has always be somebody around to represent the patients and their wishes.

Interviewer: Regarding the legal liability, how does that affect your decision-making process? In New York State, for instance, we really do have any statutes and is one of the very few states that doesn't recogni the Living Will. Does this add a different kind of pressure to your decision or not really once you've gone ahead?

Physician: No, I have practiced for the last 34 years on the assumptio that I was acting for my patients to do the best I can in their best interests. I have a number of patients who have brought in Living Wills to me. I have sat down with them, gone over it and pointed out that I'm glad to know that most physicians and I agree with them. On the other hand, I underline the phrase, " when I (the physician) do not feel that the patient will recover to a meaningful life" (or whatever that wording is). That is a judgement call. There is a gray zone that does not in any way relieve me of the major responsibility expressed in my earlier terms. It is that wrestling to decide with when do I shift gears from helping in all ways that I can for the patient to survive to that of helping them to be comfortable in their dying. That is always a difficult wrestling. But the Living Will is helpful because it gives you an opportunity to talk with the patient about their wishes as they picture them. Whether or not this has any legal standing in New York State, it has a very real ethical standing with me in guiding me in the future and have simply gone along doing essentially the same as I have for 34 years.

Interviewer: We have talked about the steps that are involved in treatin or not treating. What are the influence and authority of the different caregivers who are involved? In the nursing home you raised the issue about the importance of the head nurse. Does their input have much weight in your decision-making process or is it really pretty much up to you and how you see it.

Physician: A good head nurse or good nurse, whether in a nursing home setting or on the hospital floor, provide observations on the patient's comfort or discomfort there 24 hours a day whereas we are only there briefly. I think very important. I think many times patients may speak to the nurse about things that are on their minds which play a role in understanding where the patient is. I think there input in terms of information frequently is very important. But I don't feel that they're wishes in the decision-making process have huge weight; they're a source of information. That doesn't get me off the hook of being responsible for the decision-making.

The house staff may come up with insights or opinions that might influence me as I hear their arguments, as in all areas of medical care. They are a bright bunch and it pays to listen; and their information and their opinions may help guide you in some areas.

Interviewer: How about the family especially when it is not clear whether any prior directive has been made.

Physician: The family, I think, is always complicated by how well do you know the family. Have you known the patient for years? Has the illness been a chronic one? Have you gotten to know a family member, especially the spouse? And, always point out of course, the family has their own mixed motives: greed, guilt, anger and a whole bunch of emotions that may impact on their decision-making. I don't know whether I can always assess these correctly. If the families wishes seem unrealistic or opposed, my first loyalty ethically is the patient. If the patient has stated flatly one thing and the family are opposing, one goes with the patient. That I think is reasonably ethically clear.

For the patient that is totally incompetent, for whom you have no expression of their desire in the decision-making process, families recommendations seem to make sense so one certainly goes along with them. There are, however, a few places where you may not. If a family member came to me and requested that I not tell the patient his/her diagnosis, I have said, "I'm sorry, but my policy is that I have to level with patients in order to expedite treatment and also to keep their confidence I cannot lie to them. I try to give as much information to patients but the information that I give must be truthful.

Interviewer: Institutional committees or institutional administrators; how in your practice have they come into play at all in these decision-making issues.

Physician:

At the hospital where I do my work, we have as far as I know, not had an exceedingly functional committee. There was one appointed some years ago but I have not used them. I am not certain how much they have been used. I don't know whether its even functional at this point; its very invisible out there. What happens when there is a difference of opinion or a disagreement among the parties involved, especially with the family or the different representatives? What if there isn't a durable power of attorney? Some people have said that you have to seek out all members of the family but as soon as you get more than one you may get different opinions. Has this been a practical problem?

Physician: Obviously, it is a theoretical problem. I am not certain that I have run into this in recent years. There is usually a spouse who legally is responsible. The spouse may or may not agree with the children but I can't remember any situations where there really was spouse and children with so differing opinions that I could not resolve it. I don't think I've really faced this.

Interviewer: Are the decisions that you've made in this area of antibiot in the elderly any different if you were caring for patients with or without families. Does it still come down to whether or not they are competent or incompetent?

Physician: Again, I think one does what one, at least I do, thinks is right for that patient, based hopefully on previous conversations. I guess one ultimately does the best for that patient that one can which realistically may be imposing your value systems on them at that moment. I don't see how we can avoid perhaps projecting our own feelings at that point if life has lost its meaning and one witholds antibiotics because indeed this is what I would want for me, I believe, and what I would want for my family. You're trying to follow the patients wishes but if you don't know them, one does what one thinks one would do.

Interviewer: I have the impression that the decision regarding the use of antibiotics is different than putting an elderly person on a ventilat or starting them on hemodialysis. Antibiotics have become part of one's routine practice; they are not considered extraordinary.

It must take a very sensitive physician hold back on a treatment such as antibiotics that are effective and have relatively little toxicity. It is certainly not like cancer chemotherapy where we think a great deal. Do you see antibiotics this way? Are they different from those other li sustaining measures that we mentioned? For instance, how about food and water that some people say is fairly close.

Physician: When penicillin was a hundred dollars a gram it was extraordinary. It is not any more. There is a spectrum here. If you have g to bring the patient into the hospital to give IV antibiotics, it becomes a little more extraordinary. Whereas oral antibiotics in a nursing home setting are pretty ordinary, I agree. I think there are pressures to do the simple things for all people, and one generally does. On the other hand, just recently there was a court decision that said it may be appropriate to stop tube feeding in certain situations. So even courts, which have been the most conservative I think up until now anywa may feel it is appropriate in some instances to withold ordinary therapy It is a continuum here and obviously a large gray area.

Interviewer: Do the types of settings make the process more variable in any way? In other words, is it much easier to see what the decision-making process should be in the hospital than maybe it should be in the nursing home?

Physician: I'm not sure that there is a huge difference. There is the decision of whether or not to hospitalize that has to be made. It is easier in some ways to withold treatment in a nursing home because you don't have to involve as many people in the decision-making and convinvince them if they are not convinced. You can make the decision on your own. In a hospital setting there is a whole group of people who are involved so that setting makes it easier in terms of clarifying goals. Our goals should be set upon the basis of an accurate diagnosis and prognosis as much as possible, hopefully to --- in either side. If the diagnosis isn't clear, you may have to hospitalize the patient. The key here is the underlying diagnosis and prognosis.

Interviewer: Are there any documented policies and procedures to help you in these treatment decisions?

Physician: I guess I have internalized ethical decision-making. There are some rules about necessity of documenting in the patient's record why one decides not to resusitate. It has to be renewed every week and the note has to document that you are following the patient's wishes and that you've talked to the family. Only once, have I have written a note in the chart that I did not feel it appropriate to give antibiotics and that was my mother. She was in her 80's with severe osteoporosis, had had several strokes and was in a nursing home. While being lifted from bed to chair, she snapped her femur. She was admitted to the hospital to repair the fracture and was in considerable pain. She had been voicing for some time the wish to die but she simply was non-functional. In the course of her recovering from her surgery she developed fever and x-ray changes compatible with pneumonia. I talked to my 2 brothers and sisters and we all agreed that this (the wish to die) was her wish. It seemed that she would have a long period of continued unhappiness and discomfort. I left a note in the chart that all of us agreed that we were carrying out her wishes in not being agressive in therapy and allowing her to die. She was not given antibiotics and she did die. That is the only case that I documented in the chart of witholding of antibiotics in a hospital.

2. Brief Excerpts from Additional Interviews

A. Interview of 38 Year-Old Physician in the Private Practice of Internal Medicine:

1) How does age affect your decision regarding starting or witholding antibiotics for life-threatening infections?

For older persons I tend to have much more discussion with the patient or the family regarding how aggressive I should be in the treatment. For the younger patient I assume that there is a "fight for life". In general, I am not looking at the chronologi age but rather the physiologic age and the quality of life.

2) Mental competency...

I spend much more time consulting with the family in these circumstances. For patients who are demented I emphasize the quality of life in our discussions. The majority of our patients have Living Wills because we have been promoting this since I first started practice.

3) Are treatment decisions made differently for patients with fami

Yes, especially if the patient is incompetent. There is a substantial legal risk here which must be observed. We always t to have some legally appointed person identified. When in doubt we ere on the side of overtreatment.

4) What is the influence of the infectious diseases specialist?

We do not ask this person to help decide whether to treat o not. If we have called the consultant, we have basically alread come to the decision to treat and we are interested in knowing what are the recommendations for the proper choice of an antibio

B. Interview of 28 Year-Old House Officer in His Second Year of Residen Training in the Department of Medicine:

1) If the bottom line is the quality of life who decides whether quality is good or bad?

The patient does if he/she is competent and not depressed. Generally, we are talking about a normal functioning of bodily habits, ability to think, experience pain, etc.

2) How are families involved in making these decisions?

They are less important if the patient is competent. For t incompetent patient it can be very difficult sometimes for us. Often the patient's regular physician is not there and it is necessary to discuss some of these problems like in the middle o the night. We are not really prepared for this in our training. Sometimes it seems as though the family has different hidden agendas. We try to find out "what their feeling"on how they would want the patient to be treated. Frequently, they tell us that the patient has suffered so much that we don't want to take any aggressive actions. This comes in direct conflict with our training which has always been to alleviate suffering and to generally ere on the side of overtreatment. When we are unable to cure, and only then, do we think about comfort. Otherwise we tend to be very directing in our recommendations.

3) How much variability does there seem to be among physicians in making decisions to treat or not treat?

Many physicians never go to the family but decide the issue on their own. Frequently they will tell us "no antibiotics, I don't want to see my patient suffer any more". Some have a lot invested in their patients, become over aggressive in treatment, and see it as a failure if the patient dies. This is the case even if the family says otherwise. On the other hand, some are very involved with the family and have detailed discussions concerning their various decisions.

4) What kinds of policies or procedures or guidelines would be most helpful to you in making these decisions?

It's hard to visualize how there could be any guidelines; it seems that we always make these decisions on the basis of individual cases. If there were guidelines, I think they should be very general and maybe should be a form consisting of a number of questions. These might include: 1) has the patient been able to express their own wishes? 2) has the diagnosis been adequately made? 3) is the prognosis well-described? 4) have all avenues been explored to learn what the patient would want?, etc.

APPENDIX II-B

dnrpol2.dwb

Draft #7
10/17/88 mel

MONROE COMMUNITY HOSPITAL, ROCHESTER, NY

Title: Policy and Procedure on Treatment Preferences

STATEMENT OF POLICY

It is the responsibility of the attending physician to write an order concerning Treatment Preference for all residents/patients admitted for acute or long-term care at the Monroe Communit Hospital. Important aspects of this policy and procedure are:

1) the sensitivity to and recognition of the rights of individual residents/patients to make their own decisions concerning withholding or withdrawing life-sustaining treatments,

2) the necessary communication and documentation of the preference of competent residents/patients and

3) the necessary communication and documentation of the incompetent resident's/patient's previous wishes as provided by thei representative(s).

DEFINITIONS

1. Treatment Preferences: The following classification will be used:

a) **Hospitalization with Full Support:** A maximum therapeutic effort shall take place with resuscitation procedures, i.e., closed-chest cardiac massage, intubation/ventilation or defibrillation, in the event of a cardiopulmonary arrest.

b) Hospitalization with a Do Not Resuscitate Order: The resident/patient will receive emergency room treatment or hospitalization, if indicated, to provide temporary extraordinar therapeutic measures. He/she may be admitted to the

ICU for monitoring these therapeutic measures, which can be discontinued if the patient fails to respond. N.B.: The pati may receive vigorous support in all other therapeutic modalities and yet a Do Not Resuscitate (DNR) Order may be appropriate. [See the Policy and Procedure, Resuscitation Status: Do Not Resuscitate (attached) for further details on this order.] These modalities include administration of certai drugs, surgery, cancer chemotherapy and entero or parenteral hyperalimentation.

c) No Hospitalization Indicated: Full medical and nursing support will be provided in the long-term care areas of the hospital. This may include active medical treatment and interventions as well as laboratory investigations which are appropriate for that level of care.

d) Comfort Care: Medical treatment will be directed towards quality of life and comfort of the resident/patient. Therapeut are guided by maximizing his or her comfort regardless of its impact on the disease progress. Noninvasive medical treatments interventions and laboratory investigations may be included, un such would cause discomfort to the resident.

2. Life-Sustaining Treatments: Many different types of interventi can be life-sustaining for the elderly and chronically ill, including hemodialysis, ventilation, resuscitation, surgery, parenteral and entero hyperalimentation, intravenous hydration and medications, including antibiotics.

3. The Competent Resident/Patient: A competent resident patient, the purpose of this policy, must satisfy criteria of maturity and comprehension. Maturity means

1) an adult 18 or older, or

2) a parent of a child, or

3) a person who has married or divorced, or

4) a person who is otherwise an emancipated minor.

These persons can comprehend the nature and severity of the illness(es), the prognosis, therapeutic options available, the proba results of these options and can make informed and deliberate choices about the treatment of the illness(es).

4. The Incompetent Resident/Patient: An incompetent resident/pati for the purpose of this policy, is a person who fails to satisfy the maturity conditions above or is unable to understand the nature an consequences of his/her illness(es), is unable to make informed an deliberate choices about the treatment of the illness(es) or is unab to communicate his/her treatment preference.

N.B.: For the purposes of this policy and procedure any resident/ patient is presumed competent unless proven otherwise.

5. Representative(s): The persons listed below are considered representatives for the incompetent resident/patient and should be consulted, if available, to determine whether he/she expressed any wishes, while competent, concerning the different treatment preferences.

a) the spouse,

b) children 18 years of age or older

c) either parent

d) siblings 21 years of age or older

e) a guardian of the person

f) a relative

g) other persons, e.g., clergy, friends, etc,

GUIDELINES

1. Treatment Preferences for a Competent Resident/Patient.

The physician shall discuss the treatment preferences with the competent resident/patient and his or her wishes should be followed. No family member can overrule the decision of the competent resident/patient. The family should be informed of the treatment preferences and the physician's intention to abide by the preference unless the patient/resident requests otherwise.

There are two exceptions to this procedure:

a) suicide victims who seek to refuse treatment or

b) an adult who has dependent minor children for whom no guardia identified

In either of these circumstances, full support should be ordered.

2. Treatment Preferences for an Incompetent Resident/Patient.

a. The physician shall make a reasonable effort to contact all of the representatives and document whether the resident/patient expressed any wishes, while competent, concerning the different Treatment Preferences. If there is clear and convincing evidenc of any prior wishes for a particular treatment preference, such as comments documented by a previous physician, a recent Living Will or statements to the representative(s), this treatme preference will be considered the resident's/patient's current

b. If there is any doubt about the clarity of the resident's patient's wishes, or about his/her competency at the time of expressing same, or if there is no evidence that the resident ha previously expressed a Treatment Preference, the attending physician will document in the chart the most appropriate Treat- Preference according to his or her best medical judgment. This opinion will then be reviewed by two physicians who are not primarily involved in the resident's/patient's treatment. These second opinions, regarding attending's choice of Treatment Preference, should also be documented in the resident's/patient' record. Following this documentation, the attending physician shall consult with the reviewing physicians. This opinion will then be discussed with the representative(s).

c. If there is unanimous agreement among the representatives an the physicians, the Treatment Preference identified may be order

N.B.: Hospitalization with full support is the only Treatme Preference available for selection when

(1) a unanimous agreement cannot be reached among the representatives,

(2) the attending physician and the two reviewing physicians d not agree or

(3) there is not enough time for the process described in 2b.

d. When the Treatment Preference classification is difficult to ascertain, or when no information is available, the attending physician or representative(s) may request a consultation from a panel, the Ethics Committee. [See The Policy and Procedure, Monroe Community Hospital Ethics Committee (to be drafted) for further details on the structure and functions of this institutional body.]

e. If the incompetent resident/patient has no representative who can be contacted, the order for the Treatment Preference may be written by the attending physician subsequent to consultation by the two reviewing physicians and the Ethics Committee.

f. Even if the resident/patient was judged incompetent for a previous treatment decision, a new assessment must be made for t current treatment under discussion.

3. Implementation

After the resident's/patient's appropriate Treatment Preference is determined, this non-medication order shall be written by the attending physician. It is the responsibility of the attending physician to insure that this order and its meaning are discussed with appropriate members of the health-care team and with the new attending physician should the resident/patient be transferred.

The physician shall review and renew the order for Treatment Preference at the same interval as the other non-medication orders.

The competent resident/patient may request that the order be changed at any time. Similarly, for the incompetent resident/patient any representative may request that the current Treatment Preference order be reviewed. To ensure the greatest protection of the resident's/patient's rights, the review will include the full process described above in sections 2b-d. If there is no representative and the physician believes that the current order should be reviewed, th consultation process shall be as described in section 1e.

Nothing in these procedures should indicate to the medical and nursing staff, the patient/resident or the family or representative any intention to diminish appropriate medical and nursing attention for the resident/patient, whatever his/her Treatment Preference.

In addition, the hospital's resources shall be available to the greatest extent practical to provide counseling and other emotional support as appropriate for the resident's/patient's family as well as counseling and support measures for the care and treatment of the resident/patient.

PROCEDURE

A. Physician's Responsibilities

1. The attending physician shall discuss the Treatment Preferences with the resident/patient or his or her representatives and determine the Treatment Preference within one week of admission to the Acute Hospital Unit and within four weeks of admission to th long-term care areas.

2. The physician shall dictate the important features of the discussion as an Addendum to the type written Admission Note. Thes features include:

- a) a short description of the resident's/patient's condition corroborating the prognosis,
- b) reference to any consultations which corroborate the Treatment Preference selected and
- c) a record of the discussion(s) with the
  - 1) patient/resident concerning consent to the Treatment Preference order or
  - 2) the representative(s) concerning their recollection of the incompetent resident's/patient's previously stated desire

3. The Treatment Preference shall be written in the resident's/patient's non-medication orders and shall be updated eac time these orders are routinely updated.

4. The Treatment Preference will be recorded by the physician o the form, MCH Statement of Treatment Preference. (see E. Medical Record Section)

5. The physician should encourage the resident/patient to discuss his or her Treatment Preference with responsible family mem or main support person. N.B. The competent resident/patient has th

right to determine his or her Treatment Preference regardless of the family's wishes.

6. In the event of a transfer, it is the attending physician's responsibility to review the current treatment preference order an write the appropriate order in the MCH record. If the physician is no longer the resident's/patient's attending, he/she shall notify the new attending physician of the patient's previously expressed wishes.

7. If a resident/patient requests a change in the previously documented Treatment Preference, it is the physician's responsibility to discuss it with the resident and document it immediately in the medical record. This requires an Addendum as per A2 above, a new non-medication order and a record of the change on t form, MCH Statement of Treatment Preference.

8. If the resident/patient is incompetent, the attending physician shall establish the appropriate Treatment Preference with the representative(s) according to the best medical judgment and the prior expressed wishes of the resident/patient as noted in the section, Guidelines, Section 2.

9. If the medical condition seems to necessitate a change in a previously established Treatment Preference, it is the responsibility of the physician to discuss this with the competent resident/patient or with the representative(s), of the incompetant resident/patient. The reason for a change in the Treatment Preferen and the discussion shall be appropriately documented in the medical record as previously discussed in Guidelines, Section 2.

B. Nurse's Responsibilities

1. The nurse transcribing the original order shall enter it on the multidisciplinary nursing care plan and the comprehensive care plan. This important order will be located in a specifically designated site in each of these plans:

- Multidisciplinary Nursing Care Plan: Last two lines of treatment area on the front of the kardex.
- Multidisciplinary Care Plan: At the end of the discharge plan section on the back of the form.

2. When transcribing a renewal order of the Treatment Preference, the nurse shall check the classification as listed on both care plans and make changes if indicated. The renewal date on the nursing care plan shall be updated.

3. If emergency care is indicated, the head nurse or nursing supervisor shall check the most recent treatment preference order and relay this information to the physician.

4. If the resident/patient is transferred to another institution, the nurse will send a copy of the most recent annual history and physical Addendum concerning Treatment Preference.

5. No oral orders for a treatment preference may be taken by a nurse.

C. Social Worker's Responsibilities

1. When the family is representing the incompetant resident/patient the physician will contact the social worker, if necessary, to arrange a multidisciplinary conference to facilitate the recording of a concensus regarding the Treatment Preference.

2. This conference process will be documented by the social worker and the report placed in the progress notes.

. Other Primary Care Staff with Charting Privileges

1. When the resident/patient expresses a Treatment Preference t other primary care staff, he or she will encourage the resident pat discuss the Treatment Preference with his or her attending physician.

2. The essence of the resident's/patient's remarks will be recorded by the staff person, or their floor supervisor, in the progress note section of the medical record.

3. The physician will review the note, discuss this issue with t resident/patient and document any decisions made in the medical record.

E. Medical Record Regarding Treatment Preference

1. The initial Treatment Preference, all annual reviews and any changes will be recorded on the form, MCH Statement of Treatment Preference, which is the first page of the chart.

2. The initial Addendum regarding Treatment Preference will be attached to the Admission Note. Subsequent Addenda will be attached to the annual history and physical examination note.

3. A copy of the latest Addendum and a copy of the form, MCH Statement of Treatment Preference, will accompany the resident/patient any time he or she is transfered out of the hospita

4. The original order and all subsequent reviews of the order will be recorded in the section, Non-Medication Orders.

5. Oral orders to classify a patient may be taken and written only by a physician. Oral orders must be witnessed by at least one other individual who personally hears the order and reads and signs the documentation of the order. All oral orders must be

countersigned by the attending physician within 12 hours of the ti- given or they will be invalid.

F. Living Will

1. If a resident/patient requests a Living Will, copies will be available from Social Work or the Chaplain's office.

2. The resident/patient should be encouraged to discuss Living Will with family members and/or significant others who may serve as witness to signing.

3. Social Workers may be involved, at the patient's request to facilitate patient's reaching a decision, obtaining forms, and serving as witness. Chaplains are also available to assist and counsel as requested by patient and family.

4. A copy of the signed Living Will form should be kept in the Medical Records Department with Treatment Preference information. The original will be kept by the patient.

5. Patient and physician should review the Living Will periodically along with the Treatment Preference and update it with the resident's/patient's signature.

MONROE COMMUNITY HOSPITAL

STANDARD ADMINISTRATIVE PROCEDURE NO

Page 1 of

Date 9 1- 8-

TITLE POLICY ON RESUSCITATION STATUS: DO NOT RESUSCITATE

STATEMENT OF POLICY

It is the policy of Monroe Community Hospital that the Attending Physic shall determine the resuscitation status of a patient. A written order Resuscitation Status: Do Not Resuscitate, will be entered in the patien record by the Attending Physician only after appropriate discussion, co and documentation.

DEFINITION

Resuscitation Status:Do Not Resuscitate, means that in the event of a cardio-pulmonary arrest, no cardio-pulmonary resuscitation will be perf

SOURCE OF CONSENT

The Competent Patient

A competent patient for the purpose of this policy, is an adult 18 or o a parent of a child, or has married, or is otherwise an emancipated min who is conscious, able to understand the nature and severity of the ill and able to make informed and deliberate choices about the treatment of illness.

The Incompetent Patient

An "Incompetent" patient, for the purpose of this policy, is a patient is unable to understand the nature and consequences of his or her illnes or is unable to make informed choices about the treatment of the illness

Minor Patient

A minor patient is under 18 years of age who is not emancipated, marrie a parent of a child, and has a parent or legally designated representat

PROCEDURAL GUIDELINES

An appropriate knowledge of the patient's medical condition is necessar before consideration of an order not to resuscitate.

The Attending Physician ~~shall~~ determine whether the illness of the patie is of a terminal nature or is such that there is no reasonable chance o restoration of life or survival by the implementation of cardio-pulmona resuscitation.

Competent Patient

In the case of a competent patient, the decision not to resuscitate in event of a cardio-pulmonary event, is arrived at consensually by the physician and the competent patient. The order DO NOT RESUSCITATE is written after full discussion and agreement between physician and patie and documentation in the patient's record.

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Competent Patient (continued)

No family member can overrule the decision of the competent patient.

The patient's family should be informed of his or her decision not to resuscitate and the physician's intention to abide by it unless the pat requests otherwise.

Incompetent Patient

If an incompetent is SERIOUSLY or TERMINALLY ILL, an order not to resuscitate may be entered if family members concur in this decision. B entering such an order, the attending physician must consult with the pa family including, at least, the same family members who would be sought out to consent to post-mortem examination.

In addition, the attending physician should consult with, and have the concurrence of, the Chief of Service or his designee, before entering such orders. This second opinion as to the serious or irreversible nature of the patient's illness or his or her moribund condition should be entered in the patient's record as well as the opinion of the first physician.

When agreement cannot be reached among family members regarding an order not to Resuscitate, a Do Not Resuscitate order must be issued.

If the patient has no family who can be contacted, the order not to resuscitate may be entered by the responsible physician with the written concurrence of the Chief of Service or his designee.

Minor Patient

If the patient is a minor, the Do Not Resuscitate decision will be reached consensually by the patient's attending physician and the patien immediate family or legally designated representative.

Other

If the patient is an emancipated minor, or if the minor patient is marr or a parent of a child, the order not to resuscitate will be reached in same manner as it would be for an adult.

IMPLEMENTATION

Once the order not to resuscitate has been made, this order shall be wr as a formal order by the attending physician. It is the responsibility of the attending physician to insure that this order and its meaning ar discussed with appropriate members of the hospital staff.

MONROE COMMUNITY HOSPITAL

STANDARD ADMINISTRATIVE PROCEDURE NO

Page 3 of

Date 9 14 84

TITLE POLICY ON RESUSCITATION STATUS: DO NOT RESUSCITATE

IMPLEMENTATION continued

The facts and considerations relevant to the order not to resuscitate s
be recorded by the attending physician in the progress notes and shall
these elements; Nature of illness, a descriptive statement of patient's
competence or incompetence, source of consent (what family or patient
representative were present and/or informed), summary of discussion and
agreement reached.

The order not to resuscitate shall be reviewed and renewed at the same
interval as the non-medication orders. If circumstances change, the ord
may be rescinded at any time.

GENERAL COMMENTS

A Do Not Resuscitate order should have no impact on patient treatment or
level of patient care rendered. Do Not Resuscitate orders are compatibl
with maximal therapeutic care. A patient may receive vigorous support
all other therapeutic modalities and yet a Do Not Resuscitate order may
be appropriate.

Nothing in these procedures should indicate to the medical and nursing s
or to the patient and family an intention to diminish appropriate medica
and nursing attention for the patient, whatever his or her situation.

In every case in which orders not to resuscitate are issued, the hospita
resources shall be available to the greatest extent practicable to provi
counseling and other emotional support as appropriate for the patient's
family as well as counseling and supportive measures for the care and
treatment of the patient.

**Approved by the Medical Executive Committee of the
Medical and Dental Staff: 2/28/84**

Approved by Patient Care Review Committee: 3/9/84, 9/14/84

J. Raymond Diehl Jr.
Executive Health Administr

ANNEX NO. 7
POLICY AND PROCEDURE
ON TREATMENT PREFERENCE

MONROE COMMUNITY HOSPITAL
STATEMENT OF TREATMENT PREFERENCE

PURPOSE: This form documents the initial, all annual reviews and any changes in resident's/patient's Treatment Preference.

CLASSIFICATIONS: The following Treatment Preferences will be used:

Hospitalization With Full Support: Resuscitation procedures, close chest cardiac massage, intubation/ventilation or defibrillation, will be performed in the event of a cardiopulmonary arrest. A maximum therapeutic effort shall take place.

Hospitalization With a Do Not Resuscitate Order: The resident/patient shall receive emergency room treatment or hospitalization, if indicated, to provide temporary extraordinary therapeutic measures. The resident/patient may be admitted to the ICU for monitoring these therapeutic measures, which can be discontinued if the patient fails to respond. N.B.: The patient may receive vigorous support in all other therapeutic modalities and yet a Do Not Resuscitate Order may be appropriate.

No Hospitalization Indicated: Full medical and nursing support will be provided in the long-term care areas of the hospital. This may include active medical treatment and interventions as well as laboratory investigations which are appropriate for that level of care.

Comfort Care: Medical treatment will be directed towards quality of life and comfort of the resident. Therapeutic efforts are guided by maximizing the resident's comfort regardless of its impact on the disease progress. Non-invasive medical treatments, interventions and laboratory investigations may be included, unless such would cause discomfort to the resident.

For further details regarding classification, see the physicians non-medication order for the last date recorded below.

DATE ORDERED	CLASSIFICATION	M.D. SIGNATURE	RESIDENT/PATI SIGNATURE*

Please check the back of this page for continuation.

*Requires signature of representative if resident/patient not competent for this decision.

LEVEL OF CARE TASK FORCE

Review of Nursing Homes in Community

NAME	HAVE WRITTEN POLICY	WILL SEND MATERIAL	CONTAC PERS
Fairport Baptist	Yes	Yes	W. We Direct Soc. S
Presbyterian Home	No written policy; Co-medical directors discuss with patient and family before crisis occur.	No	M. Don Direct Soc. S
Episcopal Home	Has no written policy	No	L. Ran letta Direct
Methodist Home	No written policy; Committee formed; in process of defining levels of comfort care.	Yes Received	Marian Shack Direct Soc. S Pat Gr Direct Nursin
Jewish Home	No written policy	No	Judith Kaplan
Hill Haven	No written policy	No	V. Koby
St. Ann's	No written policy	No	Sr. Ma
State Health Dept.	Checking for written policy		Carolyn Saylor. Sajni Thadani Long Te Care Te
State Task Force - Dr. Axelrod		No.	

State checking with facilities re: clear planning for emergencies as documented for individual patient in chart. M.D. has to document prior discussion with patient and family.

State requires a written policy.

TASK III FINAL REPORT FOR OTA
OTHER ISSUES IN ANTIBIOTIC USE

I. Antibiotic Use and Development of Resistant Organisms

A. Epidemiologic Considerations.

Antibiotic use has two differing effects on the health of a population: for many people with bacterial (but not viral) infections, antibiotics can produce rapid and complete cures. But a second (more hidden) effect arises; bacteria and other infectious organisms mutate to resist the effects of man's drugs. The greater the use of antibiotics, the more likely this mutation occurs. The problem is particularly acute in situations where efficacy is reduced, e.g., urinary tract infections, associated with chronic indwelling bladder catheters in nursing home patients. This renders the drug less effective for future patients, either requiring development of new drugs or reducing the chances that doctors cure patients who had previously been curable. Perhaps the most prominent drug-resistant organisms today are from sexually transmitted diseases such as gonorrhea, but the conceptual issue is the same for any drug-treatable infection.

B. Resistant Organisms as a Cost Imposed on Others

We can think about the consequences of drug resistant organisms by distinguishing between "private" and "social" costs and benefits. Private benefits and costs are those borne directly by the elderly patient receiving an antibiotic treatment. A good example is the elderly patient with community-acquired life threatening pneumonia admitted to the hospital and treated for (say) 7 - 10 days. Initial treatment by intravenous fluids, followed by a week of intramuscular or oral antibiotics, would be common. The organism would usually be a pneumococcus, which is sensitive to several low-cost antibiotics, and a cure is obtained in 80 - 90% of such cases. The cost to others is minimal because the rapid eradication of the bacteria and the uncommon occurrence of resistance reduces to nil the change of the pneumococcus spreading to other patients in the hospital.

Yet several benefits and costs are borne directly or indirectly by others as a result of an elderly patient receiving antibiotic treatment. The eradication of a potential pathogen in the patient treated with antibiotics would reduce the changes of transmitting the bacterial to high risk elderly patients. An elderly patient with an infectious disease creates obvious costs for others when he infect them.

In addition, each use of antibiotics creates a (possibly small) social cost in the sense that it increases the rate of development of resistant organisms. The costs imposed on others can be viewed as a form of "pollution," and consideration about the appropriate patterns of use of antibiotics can and should include the effects of this "pollution". The effects may be small in some cases, and not worth the bother or cost to correct, but they may be large and important in other cases. The transmission of antibiotic resistant bacteria could be costly, especially for elderly patients, because expensive multiple-drug regimens with substantial toxicity could be required for treatment. C. A

Model to Link Antibiotic Use Rates to Development of Resistant Bacteria.

1. Biological Considerations.

The biological connection between antibiotic use rates and development of drug-resistant organisms is well accepted. Recent summaries (Levy, 1982, McGowan, 1983) show both the biological mechanism and the empirical associations of drug use and resistance. Levy notes that medical expenses increase because of the need to use two or more drugs to control infections, and states that "Despite the best efforts, deaths occur from multiply-resistant, unresponsive bacterial infections." He notes the presence of "new strains of enterococci which are resistant to all antibiotics currently available, even the most recently developed cephalosporins [emphasis added]."

While none of these totally resistant strains affect only the elderly, each can affect the elderly. We must consider the consequences of increased costs of treatment and/or premature death to the elderly from resistant organisms as an important possibility. The importance and increasing rate of resistance in nursing home populations is well documented by {citation needed}.

The empirical connection between resistant organisms and antibiotic use has been surveyed by McGowan (1983). He states:

> A causal relationship between antibiotic usage and resistance of hospital organisms is supported by consistent association and concurrent variation in several populations, presence of a dose-response pattern, and existence of a reasonable biological model to explain the relationship.

The dose-response relationship is particularly important, as will be shown below. The time between introduction of a drug into nursing homes, the hospital, or in a community and the emergence of resistant organisms varies greatly by drug-organism pairs. Occasionally, resistance emerges almost immediately, but more commonly, a drug must be used for an extended period before resistant organisms emerge. McGowan reviews a number of studies where changes in antimicrobial drug use produce parallel changes in prevalence of resistance. This relationship has been shown both when drug use increases and decreases.[1] These types of studies provide strong evidence that a dose/response relationship exists, although evidence identifying the precise relationships is lacking. Similar cross-sectional studies show higher rates of resistant organisms in hospitals where antimicrobial use is higher (McGowan, 1983).

Despite the extensive literature available, we have identified no studies that include information on age-specific rates of antibiotic use and the occurrence of antibiotic resistance. In part, this must be anticipated: the spread of resistance will depend upon antibiotic treatment rates for the entire relevant community, not just a portion (such as the elderly), and the consequences of heightened resistance can befall all groups and subgroups, including the elderly. Thus, resistance is a problem that includes both the elderly and the non-elderly, and the treatment of neither population can be considered in isolation. At the same time, it would be wrong to ignore the issue because it affects others beyond the elderly.

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[1] He cites 6 studies in hospitals where resistance increased following increased use of antimicrobials. He further reviews 16 articles showing decreased resistance following reduced use of antimicrobials.

Transmission of resistance among bacteria differs greatly, depending upon the setting. In the hospital, where antibiotic use is most intensive and contact across patients and staff with infections is most intensive, e.g., in surgical intensive care units, resistance generally spreads with the greatest rapidity. In general communities, resistance spreads less rapidly, and to a smaller fraction of a population, because of reduced contact across infected persons. In neither setting, however, are we aware of studies that include information on age-specific rates of acquiring-antibiotic resistant bacteria.

Because patients are transferred between hospitals and nursing homes, carrying with them the bacteria of the hospital, nursing homes are described as "halfway houses" for the transfer of resistant organisms between hospitals and the surrounding community (McGowan, 1983). One third of all admissions to long-term care facilities, and three-quarters of all admissions to Skilled Nursing Facilities, come from general hospitals (US Dept. of HEW, 1978). Nevertheless, little is known about the relationships between the hospitals' and the nursing homes' organisms that produce urinary tract and respiratory infections (Sherman et al, 1980).

Elderly patients in nursing homes have high rates of acquisition (and presumed transmission) of antibiotic resistant bacteria (Garibaldi et al. 1981). This study cultured the urine from 53 of 63 patients with chronic indwelling bladder catheters residing in five different nursing homes in Salt Lake City. Of those, 45 (85%) had bacteriuria. Of the 64 isolates[2] of gram-negative bacilli, 66% were resistant to first-line drugs (ampicillin) suitable for community-acquired infections, 52% were resistant to second line drugs (sulfamethoxazole-trimethoprim) and 33% were resistant to drugs reserved for life-threatening infections (gentamicin). These findings were interpreted that high-risk patients with indwelling catheters became colonized with resistant bacteria during institutionalization. However, there is some evidence to suggest that UTIs developing *de novo* in nursing home patients (as contrasted with patients transferred from hospitals) are caused by less resistant organisms (Sherman et al, 1980). This occurs because the high use of antibiotics in the hospital setting creates a more resistant class of organisms. 2. Economic Considerations.

The costs imposed by others through excess use of antibiotics can be assessed with a simple model showing the value of antibiotics to each person, the costs to each person, and the costs to others in the community. While this approach is general, it can be applied specifically to elderly populations readily. Indeed, in some settings (such as the nursing home) populated primarily by the elderly, the relevant "boundaries" and population are readily defined. To define some terms, let:

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[2] Some patients had more than one type of bacterial infection.

V_1 = the value of an antibiotic if the bacteria is not resistant (net of costs of the drug to the patient)

V_2 = the net value of antibiotic if bacteria is resistant (may be negative if drug costs are high)

P = the probability that the bacteria is drug-resistant

Q = probability that the infection is due to a species that can possibly be affected by antibiotic agents.[3]

Then the expected gain to a patient from receiving an antibiotic is given by:

$$(1)\quad E(\text{gain}) = Q*[V_1*P + V_2*(1-P)]$$

$$- (1-Q)*(\text{Price of drug})*(\text{Copayment rate paid by pt.})$$

The costs of administering the drug to society include

$$(2)\quad \text{Costs} = \text{cost of drug} + Q*X*(V_1 - V_2)*[dP/dX]/(1+r)^t$$

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[3] Viruses are unaffected by antibiotics. Yet in almost every medical community studied, large amounts of antibiotics are administered to patients with viral infections. These sorts of antibiotic uses serve to heightens resistance, particularly in closed settings such as the hospital or the nursing home. Even for patients infected by susceptible organisms, the timing of administration of the drug makes many uses of antibiotics irrelevant, e.g. if administered after the body's natural defenses have defeated the bacterial infection. Studies show that a quarter of all hospital-related antibiotic use may be useless for this reason (Shapiro et al, NEJM, 1979). A review by Kunin (1985) shows that the rates of inappropriate use of antibiotics can range from 25% to well over half of patients receiving such drugs, based on such criteria as (a) patients receiving antibiotics for viral infections, (b) in cases with no documentation or testing for bacteria, or (c) inappropriate timing. Thus the values of Q can range from .75 (at best) to .4 or lower. Kunin's own summary of this literature states that "antimicrobial agents are used for unjustified reasons...about half the time."

X represents the rate per year at which the antibiotic is used), dP/dX is the dose-response rate (the effect on the probability of resistance from changing the rate of administration of the drug), r is the discount rate. The summation takes place over all subsequent years, so long as the altered probability (P) of a resistant organism remains. For example, if (in a given community such as a nursing home) the drug is given 1000 times per year (X = 1000), and if a resistant organism persists for many years (say, 100) then the cost includes the present value of all future added costs to other patients. The future costs are discounted in the usual fashion to make commensurate costs and benefits occurring in different times.[4]

The keys to understanding how large the social costs of drug use might be are the dose-response rate dP/dX and the differences in value to patients, depending upon whether the organism is drug resistant or not. In general, these parameters are not established. We do know that the development of resistant organisms is greater for the elderly (a) in nursing homes, and (b) when transfers of patients between the hospital and the nursing home occur, especially for patients associated with surgical ICU settings than in a general community. Since there is no relevant information in the literature on these rates, we turn to a sensitivity analysis to show the potential importance of antibiotic use and drug resistance in the aged.

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[4] For very long time periods, the discounted sum is approximately the same value as a perpetuity, i.e., a stream of costs occurring forever. This sets the upper bound on the present value of a future stream of costs. In general, the value of a perpetuity equals the annual cost divided by the discount rate. Thus if the discount rate is 10 percent (r = .1) then the total present value of the perpetuity is ten times the annual cost.

3. Sensitivity Test: How Large Might the Externality Be?

What differences in the value of antibiotics might arise if a patient is infected by a non-resistant or resistant organism? Define the change in economic value to the patient (arising from having a resistant organism) as $(V_1 - V_2) = dV$. In many cases, the consequences are merely that a second (usually more expensive) drug must be administered, so dV merely reflects those added costs (e.g. $30 per patient).[5] If the patient is hospitalized, and if hospitalization is extended by one or two days due to delay in eradicating the infection, then dV includes not only the drug but also the extra hospital days (e.g, $300 per day) arising from the delay in cure. For a small number of patients, infections necessitate additional costs (e.g. surgery to drain infections that do not heal with drug administration), and for a still smaller number, death occurs directly as a result of the resistance of the organism. The appropriate value for dV is a weighted average of all such outcomes. For example, if the $30 cost (extra drug cost) is correct for 80% of patients, the $300 extra cost is appropriate for 15% of patients (one extra hospital day), $1000 extra cost occurs for 4.9% of patients (extra complications), and death occurs for 0.1% of patients (valued, say, at $1 million), then the average loss in value is $1,118. The large bulk of this cost is due to the valuation of patients who die due to resistant organisms, and the value attached to that outcome. If that fraction is much smaller (say, .001 percent), then the average loss in value due to resistance falls to the range of $150 or less. Similarly, if the cost assigned to a premature loss of life is altered, the results change similarly. In this sensitivity analysis, we look across values for dV from $100 to $1000 as a reasonable range of possible outcomes. The $100 value essentially places no cost on the chance that patients may die due to having a resistant organism.

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[5] A course of treatment with second-line antibiotics can be more expensive than "normal" antibiotics by up to $100, depending upon the drug. In one study of two drugs commonly used for treating serious infections (gentamicin and tobramycin), Holloway et al. (1984) found the average cost was about $10 for gentamicin, and about $100 for tobramycin.

These cost data are somewhat misleading. In some patients, toxic reaction to the drug created further costs, that raised the average cost per dose to $72 for gentamicin and $127 for tobramycin.

For nursing home patients in particular, evaluation of the costs of resistance will differ somewhat in approach. For example, if a nursing home resident becomes infected to the point of needing admission to a hospital to monitor a serious infection, then entire costs of the hospitalization might be attributed to that infection. Naturally, if the infection is resistant, then the added costs of the hospitalization (compared with the nursing home costs) enter the cost calculations.

Some of the costs of resistant organisms are wholly subjective, and may differ for the elderly, disabled, and terminally ill nursing home patient populations, compared with other groups. Some elderly patients, when confronting the choice of extensive and painful therapy (for example) for cancer, choose an alternative setting such as the hospice, where comfort and quality of remaining life replace medical treatment as the goals. For such persons, the consequences of a resistant infection may differ greatly from persons who prefer an active and aggressive treatment. In establishing values for this sensitivity analysis, we in no way suggest that one choice is more appropriate than another, but merely show the consequences for appropriate antibiotic use under differing situations.

The other key issues include (1) how long does the enhanced probability of resistance persist, (2) what is the dose-response rate of drug use - drug resistance, and (3) what discount rate should we use for costs occurring in the future? We can restructure Equation (2) above to show the net effect: Let $e = [dP/dX]*[X/P]$ = the percentage change in the probability of an organism being resistant following a one percent change in the level of antibiotic use. Then Eq. (2) becomes:

(3) Damage = $[P * Q * dV * e] /(1+r)^t$

In this very simple model, the extra societal penalty arising from any use of an antibiotic is the product of the expected loss in value of the antibiotic times the proportional effect of the drug use on microbial resistance. Thus, with knowledge of P and Q, we can parameterize dV and e to see what range of damage might arise annually. We can then add up across the number of years for which the heightened resistance remains, to determine the total costs of enhanced drug use.

From the literature (see footnote 3), Q is approximately .5: half of all patients receiving an antibiotic should not have been treated by the drug. The literature also tells us that the probability of any organism being resistant to a drug varies greatly across cites and through time. Approximately 20% of all hospitalized patients may be affected by some bacterial infection. (Data in Shapiro et al, 1979 from a randomly chosen group of hospitals shows that 30% of patients received antibiotics, and about 70 percent of those were not for prophylaxis. Thus by inference, approximately 20 percent had infections.) The key question is, what fraction of those infections are resistant, and how does that fraction change with greater drug use? In some cases reported in the literature, up to 80% of all infections are resistant to at least some drugs (McGowan reports a number of such studies). He reports that resistant organisms account for 7% of all urinary tract infections in several studies. Levine et al. (1985) report that aminoglycoside resistance in the major pathogen causing urinary tract infections varied from 2 - 6% for the most powerful drug (amikacin) to 10% or more (tobramycin) and 15 - 20% or more (gentamicin).[6] As noted above, one study of nursing home patients with indwelling catheters found higher rates of resistance, with 66% showing some resistance, and up to one third of these resistant to even the more powerful drugs such as gentamicin. In subsequent sensitivity analysis, a value of 10% will be assumed for P, the fraction of all organisms that are resistant to drugs, but this number can clearly be higher (and hence the problem worse) in elderly patients with particular infections. The choice of the 10% value allows easy rescaling of results to other levels. For example, in cases where the true rate of resistance is 20%, a simple doubling of the numbers in Table III-1 analysis is appropriate.

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[6] The large difference across these studies reflect the inherent nature of resistance mechanisms in bacteria; the rate at which resistance will occur depends upon the particular setting, the extensiveness of antibiotic use, and even upon such things as the precautions taken by medical personnel to prevent cross infections. This does not deny the validity of the individual analyses, but merely points out the importance of assessing individual circumstances.

The potential range of damage caused annually by any dose of antibiotic can now be crudely measured. Let the loss in value of the drug range between $100 and $1000 (as discussed above). We will similarly vary the parameter e from 0.1 to 1.0.

Recall, when $e = 0.1$, a 1% increase in the rate of antibiotic use increases the chances of resistance (relatively) by 0.1%, etc. This parameterization approximately surrounds the few sparse pieces of evidence on the actual number in the literature, but may be conservative. We have used data in Levine et al. to estimate the relevant elasticity for gentamicin and amikacin use and resistance rates. Using data in their figures 2 and 3, the relevant elasticity was estimated at .15 for gentamicin, statistically significant at the .05 level. A regression of their data on amikacin resistance yielded an elasticity estimate of 1.1, significant at $p < .001$. By contrast, other studies cited by Levine et al, show no correlation between amikacin use and the development of resistant organisms. Our parameterization of e = .1 to 1.0 approximately spans this range of estimates.

[Table III-1 about here]

The values towards the top of Table III-1 are more appropriate whenever the organism does not cause death, even in badly resistant cases. The values towards the bottom of the table reflect the situation when a life is valued at $1 million and 1/1000 infected patients dies. Particularly in these latter circumstances, these results are quite startling: the costs imposed on society appear to be on the order of $5 to $50 each time antibiotics are used if resistant infections kill people at a rate of 1/1000 infections, given the value of life assigned ($1 million).

Data in Table I-2 (Task I) show the rates at which patients with various medical devices develop infections, and the rate at which those infections are fatal. By far the most frequent infection source is a urinary catheter, where almost 200,000 elderly patients per year have the device, and an estimated 20 percent of these will develop infections. Of those infections, less than 1% are thought to cause fatalities. For other more invasive procedures, the infection rate is often the same or smaller, but the fatality rate among those infected is much greater, often 20 to 40 percent. Thus the assumption of a 1/1000 fatality rate may greatly understate the actual circumstance. Thus, even for those believing that the $1 million valuation of life is inappropriately high, the expected values of costs may be higher than these calculations suggest.

If a higher fraction than 10% of all infections are resistant (larger P), these costs rise proportionately, and conversely. In the United States, the annual number of antibiotic prescriptions written apparently exceeds 150 million[7], the external social costs accruing annually in the United States (using the range of values from Table III-1) would appear to be at least $75 million and may be as high as $.75 billion or more.

The total social costs of an extra antibiotic use are the sum over all future years where the extra resistance persists, discounted appropriately. For many such issues, a discount rate in the range of 5 to 10 percent is used, reflecting the opportunity cost of capital to society (the value in its best alternative use.) This means that, as an approximation, if an increased resistant organism persists for many years, this means that the true social costs of using an antibiotic are 10 to 20 times those costs given in Table III-1.[8] The literature on resistant organisms suggests that once resistance develops, it tends to persist for long periods (McGowan 1983, Levy, 1982, 1983). This means that the true social costs from antibiotic prescriptions may be as high as $.75 billion to $7.5 billion. If the resistance lasts 5 years, then the costs are still 4.2 to 4.5 times those in Table III-1, and the total social costs of 150 million prescriptions in the US annually could range from $.3 billion to $3 billion.

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[7] Over 100 million antibiotic prescriptions are written annually in office practices (US Dept. of Health and Human Services, April 15, 1983). In hospitals, 43% of all discharged patients are estimated to have received antibiotics (Kennedy, Forbes, Baum and Jones, 1983), adding another 18 million antibiotic dosages annually, although there is wide variation across hospitals. (For example, Durbin et al. (1981) estimated that 68% of all surgical patients received antibiotics in one hospital, while Maki and Schuna (1978) estimated that 26% of all medical/surgical patients in another hospital received at least one course of antibiotics.) The use rate of 43% contrasts with the reported rate of infections of 20% (derived from data in Shapiro, 1979), lending further support to the hypothesis that much use of anti-infectives is inappropriate.

Baum, Kennedy, Forbes, and Jones (1985) report prescriptions for the top 25 selling pharmaceutical. Of those, 6 drugs were antibiotic agents, and those six alone accounted for 137 million prescriptions. Thus the annual rate of antibiotic prescriptions would appear almost certainly to exceed 150 million.

Within the elderly, antibiotics are not the most common drug, but are still widely used. Lamy (1980) estimates that 17% of all residents of Skilled Nursing Facilities receive anti-infectives. But beyond this, no information appears available on the actual use of antibiotics by the elderly.

The importance for the elderly populations of the United States for this issue are considerable. While the elderly are a relatively small fraction of the population, they form a much more substantial fraction of the hospitalized population, and almost all of the nursing home population of the country. Since the spread of resistant organisms is known to be faster and more extensive in these settings than elsewhere, the elderly could bear a significantly disproportionate share of the costs of resistant organisms. For the chronically and terminally ill patient, the problem may be even worse, because of diminished natural ability of the body to combat infections. Patients undergoing chemotherapy may be particularly susceptible to the problems of resistant organisms.

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[8] See footnote 4.

This exercise is merely a sensitivity test, and while based in part on data in the literature, is not a definitive study of the issues. The range of values for extra costs imposed by resistant organisms is plausible. However, better information is needed on the dose-response pattern of drug use and development of resistant organisms. If the range of drug response relationships used is even partly appropriate, and particularly if the duration of heightened resistance is long (as the literature suggests is the case), then these simulations suggest that the external costs of antibiotic use may be much larger than has been previously suspected. With this in mind, we turn to discussions of ways to reduce or control use of antibiotics.

Options to Alter Rates of Antibiotic use

Antibiotic use can be affected by changing the prescribing habits of doctor, the care-seeking habits of consumers, or the incentives facing either the doctor or the patient. Mechanisms available to undertake such change include the following:

1. Information to providers. Changing the prescribing habits of doctors has been addressed by a number of professionals. Information conveyed through package inserts, advertising, and professional journals and meetings all offer the opportunity to alter these habits. We must recognize that information that reduces the frequency of prescription of a drug runs counter to at least the short run interests of the pharmaceutical industry. Kunin (1981) reviews nine mechanisms to alter the prescribing behavior of doctors in the hospital setting, all of which effectively

alter the information the provider either has or must supply before certain antibiotics can be prescribed. The mechanisms include: Education programs, control of contact between physicians and pharmaceutical salespersons, limitations on hospital formulary, provision of sensitivity tests from microbiology laboratory, and a series of requirements for consultation and approval before more high-cost agents are used. The mechanism by which each might work differs; the least obvious is the effect of sensitivity test information given to physicians. These tests help the doctor determine if the drug he is considering will actually affect the organism of a particular patient, and thus will help eliminate drug therapy regimens that are ineffectual.

The influence of drug salespersons on drug use is shown both to be significant and larger than physicians recognize (Avorn, 1983). A mechanism of "counter-detail men" to provide information of non-efficacy to doctors has been shown to counteract these effects (Avorn and Soumerai, 1983).

These mechanisms center on the hospital as a locus of control of prescribing patterns. While this can have significant effects on the prescribing patterns affecting the elderly, it will not likely have significant effect on behavior in nursing homes or other sites where the elderly receive antibiotics. However, altering the financial incentives to prescribe antibiotics has been remarkably effective in some settings (see discussion below at item 3) that may prove more important in the nursing home setting.

2. Information to consumers.

Much medical literature is devoted to the notion that doctors prescribe antibiotics as the easy way to deal with patients. Patients are said to expect and even demand prescriptions for many occasions when they are not warranted. When both the patient and the physician feel that the antibiotic is harmless, it is often the easiest thing for the doctor to proceed with the prescription. Thus, information to consumers may help.

Recent analysis of patient package inserts has shown that consumers can and do make use of even relatively complicated information, and discuss therapeutic choices with their doctors more when given such information (Kanouse et al, 1981). If patients were better informed about subsequent personal risks of acquiring a resistant organism when they increase their frequency of antibiotic use (which is well documented; see McGowan, 1983) it may change their attitudes toward seeking and accepting antibiotic prescriptions. While some elderly have reduced capacity for decision-making, many have competent relatives or friends who advise them. This will especially be important for elderly patients who frequently receive antibiotics for asymptomatic urinary tract infections.

Special issues arising with the elderly in this approach include the possibility of providing patient inserts with particularly large type and illustrations (to improve readability). and the role of health providers in supplying this sort of information to elderly patients and their families. While patient package inserts provide their greatest role in outpatient drug use, it is possible to invoke patient choices even in the inpatient and nursing home setting. If patients are not competent, alternative decision-makers can substitute for the individual.

3. Peer review. Brook and Williams (1976) have shown that peer review, coupled with denial of payment for inappropriate medication, can greatly reduce the frequency of inappropriate medications. Their study of the New Mexico Medicaid program studied the out-of-hospital rates of prescribing antibiotics of participating doctors before and after a peer review program was introduced. The Medicaid program hired doctors to review prescription patterns, with particular emphasis on antibiotics. Payment for charges associated with injections (for example) was denied when there was no documented evidence of bacterial infection. The rate of inappropriate injections by up to 60 percent after the review was instituted. (Brook and Williams, 1976). For antibiotics in particular, the fall in use was striking. As the program was initiated, about one-quarter of all antibiotic injections were denied for medical inappropriateness. Despite this relatively low denial rate, use of short-acting penicillin declined two-thirds, and use of other more powerful antibiotics fell by 65 to 80 percent. Thus, peer review through reimbursement systems seems to have potentially powerful effects on prescribing behavior of physicians.

General guidelines for peer review of and specific indicators for antibiotics have been developed by Kunin and Efron (1977), although the long term effects of ongoing review in the hospital setting (independent of reimbursement mechanisms) is unknown. Further, administering such programs in the nursing home population may prove much more difficult than in hospitals, suggesting that the only effective mechanism may be through payment plans such as studied by Brook and Williams.

4. Patient Copayment and Reimbursement Choices.

It is well established that reimbursement affects patient demand for drugs in general. Studies reported in Phelps and Newhouse (1974) show that the numbers of prescriptions filled by patients does change quite significantly when the insurance coverage varies. In one case, prescriptions for a Medicaid population approximately doubled when insurance coverage was extended. In another case, an insured population received almost double the population of a comparison uninsured group. And in a third study, the prescription rate in the British National Health Service fell by approximately 15% when the equivalent of a $1 copayment (approximately) was introduced for a period of time.

None of these studies deal specifically with antibiotics, and none deal specifically with the chronically and terminally ill. We can only expect that -- as with other medical services -- sensitivity to price will be larger in an ambulatory setting, and likely very small in the inpatient setting (Newhouse et al, 1981). This analysis is substantiated both by the lower responsiveness of inpatient treatment patterns to price (Newhouse et al, 1981) but also by the very broad and complete coverage of inpatient services (HIAA, 1985).

5. Quotas or limits on aggregate use. Particularly in the inpatient setting, methods to limit use of antibiotics may have to employ novel approaches. One approach used elsewhere is to limit the overall amount of the product that can be used by administrative decision, allowing individuals to decide where to use the artificially scarce resource. The entire British National Health Service is characterized by such methods: deliberate limits set on resources available, with physicians making decisions about access to those resources. While such techniques have not commonly been employed with antibiotics, there is no reason in concept why they could not be used. Kunin (1981) notes that formulary committees of hospitals can help evaluate claims of pharmaceutical manufacturers as method of controlling which agents are made available in the hospital. However, it seems unlikely that a hospital formulary could afford to wholly eliminate classes of antimicrobials from the hospital, and the formulary cannot control individual use patterns.

Some programs have required consultation by infectious disease specialists for continued use of antibiotics, or even for initial use of the most expensive and powerful antibiotics. One study (McGowan and Finland, 1974) demonstrated that the requirement for a written justification of antibiotic use alone reduced use of these drugs. These approaches seem effective at least in the hospital (Kunin, 1985) but the ability to use them in the nursing home setting has not been demonstrated.

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Title: Life-Sustaining Technologies and the Elderly:
Antibiotics and the Elderly

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6. Medical malpractice law. Malpractice law probably has little effect on antibiotic use now. Effects of malpractice law depend upon the establishment of a standard of care upon which the courts can rely for comparison. In general, such a standard does not exist, although work in the VA setting (Jones et al. 1977) offers a first approach to this. If anything, tendencies to increase antibiotic use probably arise, particularly for post-surgical "prophylaxis" as a "defensive medicine" strategy. Risks of under-prescribing seem potentially severe: if a patient is harmed (for example) by a post-operative infection and antibiotics have not been prescribed, the doctor is quite likely to be held liable. On the other hand, if a resistant infection develops, due to previous over-prescribing of antibiotics or simply through nosocomial infections, the evidence will likely be very weak, and the opportunities for a patient to sue successfully seem minimal. While we do not have the resources for an review of case law in this issue, the economic aspects of the malpractice law seem to lead to higher, not lower rates of antibiotic use.

Any federal role in malpractice law must be indirect, since the tort liability law differs from state to state, and there is no pertinent federal law. Thus, for example, any attempts to extend the guidelines established in the VA setting (Jones et al., 1977) must rely upon state action. Any federal role can only emerge through (for example) the setting of "model laws" or standards which the states can choose (or not) to adopt.

II. Reimbursement Issues affecting Antibiotic Use

A. Spending and reimbursement for antibiotics (data review).

Annual spending and insurance reimbursement on drugs have been documented independently by Baum et al (1985) and from surveys undertaken by the National Center for Health Statistics periodically. At wholesale prices in 1983, anti-infectives accounted for $1.9 billion in sales, about $1 billion in hospitals and the remainder in drugstores, the latter being by far the most common source of drugs for nursing home patients. (If the nursing home were to maintain its own pharmacy, it would require a pharmacist present; few choose to do this. Some nursing home patients bring significant supplies of drugs into the nursing home from hospitals.) Antibiotics account for one third of hospitals' expenditures for prescription drugs. (Baum et al., 1985).

Reimbursement for prescription drugs in general is low, compared with other medical care services and goods (Kaspar, 1982), both for the under-65 population (private insurance), which pays for only one-quarter of the costs of prescriptions for this population and for Medicare and Medicaid on behalf of the elderly, which together pay for the same fraction of the costs of prescriptions as private insurance does for younger persons.

No direct evidence is available regarding insurance and out of pocket costs for antibiotics, but we can infer that insurance in fact pays for a much larger fraction of these drugs than for all drugs in general. Both for private insurance and for Medicare, drug costs will be almost fully insured when acquired as a hospital inpatient. (Medications obtained while not in the hospital are not covered under Medicare Part B, but are covered under almost all state Medicaid programs, for which a significant number of elderly are eligible.) Since hospitals account for one third of all antibiotic prescriptions and over half of all antibiotic expenditures nationally (Baum et al., 1985), the average insurance benefit for antibiotics must be correspondingly high. In addition, over half of all Medicare participants purchase private supplemental insurance (HIAA, 1985), providing further insurance benefits for outpatient drug purchases. No information is available to ascertain the extent of such drug payments in general, let alone information specific to the use of antibiotics.

B. Incentives for Antibiotic use in DRG system

Payment for hospital care is now transforming under the new Diagnostic Related Groups (DRGs) from payment per unit of service to payment per admission. Consideration of physician-based DRGs is underway and the potential for DRG-like payment in nursing homes is also obvious. (Indeed, payment for nursing homes in some states, including New York, already uses such approaches.)

In any of these settings, a DRG approach to payment may have little effect on antibiotic use, and indeed, it could possibly accelerate the rates of use in some settings. Consider the hospital as a prototype: The fundamental incentive under DRGs is to shorten length of stay whenever possible. Since the cost of a course of antibiotics (even the relatively expensive types used in hospitals with resistant organisms prevalent) is very small relative to extending a hospital length of stay, there may be significant pressures to increase the use of prophylactic antibiotics (e.g., post-surgical, decubitus sores, etc.) as a precaution against extended stays. Because such patterns of drug use may create resistant organisms and eventual lengthened stays, hospitals will need to develop new methods of oversight to evaluate the effects of antibiotic use in their own settings. Since the literature seems to indicate a widespread overuse of antibiotics under current practice, hospitals may well find it in their own interest to establish surveillance committees internally as a way to combat the eventual development of resistant organisms.

Some surgical procedures explicitly allow higher payment (different DRG) for "extended complications," in which case the financial consequences for the hospital from an infection may actually be positive.

We have to date been unable to find evidence relating to antibiotic use before and after DRGs were introduced. The more extended period of DRG use in New Jersey and Maryland suggests that these states will provide the best evidence, if any becomes available. Data from New Jersey are available on length and frequency of hospitalization under the DRG system, but no studies have appeared addressing more detailed topics such as antibiotic use.

III. Possible Federal and State Interventions

A. Concerning drug-resistant organism development

1. FDA rules on information. As discussed above, the information available to physicians (package inserts) and patients (patient package inserts) can be controlled by the FDA. If so desired, the FDA could modify the inserts, highlighting more the consequences of antibiotic use not only for development of resistant organisms in the individual person, but also the more complex "civic" problem of resistant organisms development affecting others.

2. PRO law. Under the DRG system, Medicare has relied more intensively on peer review. While many view the Peer Review Organizations (PROs) as devices to limit or control hospital length of stay, these organizations could be used to study antibiotic within any hospital, and even by individual physicians.

3. Medicare and Medicaid reimbursement. Particularly in the inpatient setting, there seems little potential for these public insurance plans to control antibiotic use through reimbursement as it affects the patient. Within the hospital, drug expenses have been covered, and under the DRGs, the payment to the hospital is independent of their use of antibiotics directly.

The alternative approach would alter the reimbursement paid to physicians, depending on the appropriateness of their prescribing patterns. Physicians have been shown to respond to changes in reimbursement in one Medicaid program where the specific aim was to alter patterns of antibiotic use. Particularly when coupled with the PRO review process, Medicare could adopt the same process, at least for the inpatient setting.

4. State malpractice law. Previous discussion of malpractice law centered on the risks facing a physician for not administering antibiotics. Modifying state law to recognize the effects of antibiotics on development of nosocomial and resistant infections could provide some protection to physicians who choose a different medication strategy. Conversely, development of case law that found physicians and hospitals liable for not having a program to control the use of antibiotics (as a measure to reduce and control the prevalence of resistant organisms) could provide similar pressure to modify prescribing behavior.

5. FDA analysis of drug use patterns. Antibiotics fall only under the standard FDA guidelines demanding proof of safety and efficacy. Aside from approving general patterns of use, the FDA rules do not affect individual choices of drugs by doctors.

As with many other issues in antibiotic drug use, much critical information is not available. Very little has been developed to directly assess the critical dose-response curves linking antibiotic use to resistant organisms development. Such studies, as a part of the FDA's mandated control over the safety and efficacy of drugs, could prove very important. Such studies fall outside of the standard FDA approach, since they would be primarily epidemiologic in style, rather than relying on controlled experiments of drugs for safety and efficacy. However, if the information begun to be developed by Levy, McGowan, and others were sustained and improved with further studies, it seems likely that the broader considerations of "safety" and "efficacy" regarding antibiotic use might be revised. While the FDA primarily studies the safety of a drug for individuals, the studies needed here relate to the safety of entire communities as drug use patterns change. Clearly, a large scale study would be needed to assess this problem fully.

TABLE III-1

ANNUAL COSTS OF A SINGLE TREATMENT WITH ANTIBIOTICS FOR VARIOUS POTENTIAL SITUATIONS

		Percent Change in Resistance Rate due to 1% Change in Antibiotic Use*				
		0.1	0.25	0.50	0.75	1.0
Loss in Value of Anti-biotics due to resistance (dV)	$100	$.50	$1.25	$2.50	$3.75	$5.00
	$250	$1.25	$3.12	$6.25	$9.37	$12.50
	$500	$2.50	$6.25	$12.50	$18.75	$25.00
	$750	$3.75	$9.37	$18.75	$28.12	$37.50
	$1000	$5.00	$12.50	$25.00	$37.50	$50.00

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*See formula in text. Assumes that 10% of infections are resistant (P = .1) and half of all uses of antibiotics are inappropriate (Q = .5).

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TASK.IV DEVELOP GUIDELINES FOR DECISION-MAKING FOR DIFFERENT TYPES OF PATIENTS IN DIFFERENT SETTINGS

In this Task we have briefly outlined our suggestions for guidelines to reduce the variability in how treatment decisions are currently made regarding antibiotic use in the frail elderly. ~~In formulat~~ing these guidelines we have considered the many problems that care-givers commonly face in treating critically or terminally ill elderly patients. It should be noted at the outset, however, that the goal of reducing variability in how treatment decisions will probably have both good and bad consequences. Good consequences will result from improving the physician's skills in the diagnosis and treatment of elderly patients with bacterial infections and providing a structure for physicians to discuss with the patient and family, all aspects of the decision to treat or not treat with antibiotics. Bad consequences will result because rigid guidelines (? statutes/codes) will severely limit the individual capabilities of the best physicians, already sensitive advocates for their patient's wishes to practice the art of medicine. That art depends on the individual physician patient relationship.

Medically-oriented Guidelines. From the medical perspective, treatment decisions are primarily influenced by the multiple constraints under which physicians work and the pressures that are exerted on them to prescribe antibiotics. Some of the major factors that appear to influence the physician have been recently summarized [Figure IV-1; (Kunin, 1981) and Table IV-1 (Kunin, 1985)]. A principle component in many of these factors is the fear on the part of the physician of failing to provide patients with the very best drug for a presumed infection. With the development of remarkably effective antibiotics against most bacterial pathogens, Kunin and colleagues (1973) described the times as the era of the "drugs of fear". And although many lives have been saved by these drugs, the underlying conditions that precipitated the infection have not been resolved. In many cases, therefore, drugs have been used without effect or simply delayed death (Kunin, 1985).

Several methods for controlling the use of antibiotics in hospitals have been proposed [Table IV-2;Kunin (1981)]. A few of these methods will be discussed to emphasize their use as guidelines for decreasing the variability of treatmentdecisions.

1. Physicians have major deficiences in the knowledge of antibiotic use (Neu & Howrey, 1975) and the proliferation of new second, third and fourth generations of subclasses of various antibiotics has caused even more difficulties. Continuing medical education programs can be used to develop guidelines for appropriate use of antibiotics but, when tried in hospital settings, results have been both effective (Achong et al, 1977) and ineffective (Jones et al, 1977). Minimum criteria for the selection of appropriate specific antibiotics (Appendix IV-A) have been developed by Zimmer and colleagues (1985) to assess antibiotic usage in the nursing home setting. These criteria could be

developed as guidelines for physicians in nursing homes in general and linked to other quality assurance programs as required by third party payers.

2. Kunin (1981) believes that the most important aspect of education is to familiarize the physician with how to improve the diagnosis of bacterial infections that might require antibiotic treatment. Once proper diagnostic techniques are mastered, information about the use of specific antibiotics can be provided. Kunin (1981) suggests that several techniques will enable the physician to be more confident in his/her diagnosis and to defend more accurately cases that require antimicrobial therapy. These include:

1) the use and interpretation of gram-stained prepartions of aspirates of abscesses and respiratory secretions,

2) recommended procedures for obtaining urine and throat cultures and

3) frequent use of blood cultures for febrile patients with elevated white cell counts.

Diagnostic studies are usually performed in hospital settings but frequently omitted in the management of suspected bacterial infections in residents/patients in nursing homes (Zimmer et al, 1985). Recommendations for routine diagnostic work-ups in this setting have been proposed [Appendix IV-B, (Zimmer and colleagues1986)]. These recommendations were more demanding than the criteria used in the previously quoted study (see Task 1, Section VII) and were designed to upgrade care practices. Because of the constraints on diagnostic capabilities in long-term care facilities, these guidelines would require modification and adaptation best suited to the needs of the local practicing physicians.

These guidelines, together with guidelines on the minimum criteria for starting antibiotics (Appendix IV-C (Zimmer et al, 1985)), could form the basis for a nursing home-based medical audit. Such an audit would be developed by the Medical Director and Pharmacist and would establish standards of antibiotic usage based on local needs and judgements but guided by independent criteria. The physician's prescription would initiate the audit which would be performed by the utilization review team, infection control officer or a trained staff nurse. This procedure would measure compliance with local standards and provide feedback to the nursing home Medical Director and physician staff members regarding instances where physicians fail to adhere to guidelines adapted by their peers. In addition, as suggested by Kunin (1981), increased emphasis on procedures that are used in the diagnosis of infectious diseases could also be encouraged if their costs were paid directly to the physicians by a third party.

Process-oriented Guidelines. These medically-oriented guidelines, directed toward improving the physician's understanding and use of antibiotics, are valuable but focus primarily on the technical aspects of optimal use of antibiotics in elderly patients, including reduction of inappropriate use. The process of deciding questions of antibiotic treatment in elderly patients, is not, however, only a narrow medical matter of fitting a medication to a diagnosed illness. It is, in addition, a broadly medical-ethical matter which involves the patient's wishes, the patient's family, the patient's physician and various other caretakers, especially the nursing staff. Additional factors affecting the decision include laws and customs of both the immediate institution and the geographical region in which the decision takes place. Nevertheless, it is possible to identify guidelines that are process-oriented with the goal of assuring, as much as possible, that the physician has carefully considered the goals for starting the antibiotic and that these goals are consistant with the patient's individual rights and previous wishes.

The Policy and Procedure on Treatment Preference from the Monroe Community Hospital [Appendix II-B; Monroe Community Hospital (1985)] illustrates well the responsibilities of the physician as well as clarifying the roles and responsibilities of the family and other caregivers. From this a number of general guidelines can be identified for reducing variability in how treatment decisions are made. Examples of these are:

1. The wishes of a competent patient in consultation with his/her physician are to be followed in regard to treatment decisions. Advance directives or prior wishes are to be followed only when patients are no longer able to engage in the decision-making process.

2. The benefits and burdens of therapy must be calculated for the dying or irreversibly comatose patient who has left no advance directives ([illegible], 1985). Families are to be consulted in these decisions. The wise physician confers with staff (Hilfiker, 1983; Hunter, 1985), particularly in a nursing home, where nurses assume a greater role in the decision-making process. The services of the clergy, social workers, an ombudsman, and an ethics committee may be needed to resolve conflict among family, between family and staff, or among staff.

3. Education of the public about the nature and prognosis of medical conditions and the advisability of declaring one's wishes in

advance of incapacity is needed. Long-term care facilities will do well to establish plans for each patient's care in the event of irreversible, terminal illness (Levenson, 1971, Mott P. and Barker W., special subject in OTA Contract (Antibiotics): Witholding/Prescribing Antibiotics in a Nursing Home, 1985).

4. Physicians heeding patient's wishes in regard to forgoing antibiotic treatment in the last stages of life require--or believe they require--legal protection. Most of the Natural Death Statutes in the 36 states that have such legislation specifically refuse to provide legal immunity for physicians, nurses, and health care institutions that will enable them to follow patient's directives to withold antibiotics. Therefore, if legal protection is to be provided for witholding antibiotics, these statutes would require substantial amendment. To the extent that legislatures are unwilling to provide broad immunity for witholding medicines, including antibiotics via a Living Will, they may be willing to do so when the prior directive is a durable power of attorney. Legislation is needed in the remaining 14 states.

5. These guidelines must be flexible, realistic, capable of reflecting the patient's and the family's wishes regarding treatment decisions and consistent with the local medical and bioethical standard for high quality care. The latter is essential if physicians, in general, are going to support this process. Careful drafting of legislation is, as the President's Commission noted (at p. 153) necessary to "balance provisions arrived at restricting likely abuses and those intended to allow flexibility and individuality for patients and proxies.

Types of Patients. The types of patients who probably would most benefit

IV-0

by these guidelines would be the frail elderly person and those who are cognitively impaired and without their own physician, family or other advocates. The best setting for implementing these guidelines is probably in the nursing home where these patients frequently live out their lives. In this setting, there is regularly the dilemma between cure and care and extending life versus extending death, occurs regularly.

Implications. Some of the implications of these guidelines are:

1) A decision-making structure will be created that includes the interests of patients and their families in the treatment decision.

2) Elderly persons with no families will require a special guardian/proxy.

3) The medical-legal guidelines will specify that care-givers will consider the patient's wishes or advanced directives.

4) Appropriate Natural Death Statutes must be drafted in a more comprehensive manner to include medications (specifically antibiotics) so that physicians, other care-givers and institutions have no fear of legal liability. Antibiotics should be considered "extraordinary" treatment only when a non-treatment decision has been made.

5) Most importantly, these guidelines will promote active participation by all parties and improve the understanding of the consequences of the decisions.

6) Finally, it should be noted that these process-oriented guidelines may actually increase the variability in the treatment decisions. This is because presently most physicians believe that everyone should receive antibiotics and that this is always "appropriate" when an active infection is present. The guidelines would increase the variability in outcome, i.e., treat or withold antibiotics, but should provide a standard of practice/process by which the outcome is reached.

Federal Role in Implementation. Increased acceptance of these guidelines could be accelerated by several Federal government actions. First, increased acceptance could be promoted by educational efforts to increase public awareness of these concepts and procedures. This could include material made available by mail to consumers and doctors, or through organized symposia for medical and administrative personnel throughout the nation.

Second, these guidelines could be embodied in medical practice codes, and some potential federal effort arises here as well. For example, if the various state malpractice laws specifically offered compliance with these guidelines as a defense against malpractice suits relating to antibiotic use, their use would expand and more people would become aware of the concepts just through this mechanism. One federal role arises through the mechanism of "model statute."

Financial incentives could also increase acceptance and implementation of these guidelines. For example, the current scope of benefits in Part A of Medicare discourages physicians from admitting patients to nursing homes and emphasizes frequent referrals to the hospital. Most importantly, the Part B fee schedule does not compensate well for "cognitive services", including counseling that is much-needed to implement these guidelines well. Current reimbursement for hospices includes palliative and comfort-giving care. Parallel reimbursement for physicians in other settings would enhance the frequency with which such counseling and consultation is provided.

In conclusion, we hope that our report on the Decision-making Process Regarding the Use of Antibiotic Treatment of Elderly Patients will be read with a broad context in mind. The development of government-sponsored rigid guidelines that utilize arbitrary age boundries, mandatory treatment for those able to score highly on mental status questionnaires, denial of treatment for those unable to achieve such scores or other systems which contain little or no flexibility or ability to respond to the patient's or family's treatment preferences, would not suit the needs of any of the partyies involved.

To restate a previous concern, the reduction of variability may have important consequences of a negative nature for the practice of medicine. We believe that the best, most caring physicians, who act as patient advocates rather than technicians, may suffer the most. Loss of the capacity to make professional decisions on the very specific facts of each case is a real loss--especially for private practitioners and especially in the community or acute care setting.

Finally, we strongly urge that cost-containment policies and programs not be promulgated for older persons solely because of their age (or economic condition), as has tragically begun in Great Britain. There is an unspoken danger when one group isolates another group and decides who shall live or die. The goal of our guidelines is to increase the education, communication and sensitivity among physicians so that they, and other caregivers, can focus better on one of the most difficult areas in medicine and for society.

Task IV.
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Figure IV.1 Multiple Constraints and Pressures That Are Exerted on Physicians to Prescribe Antibiotics.

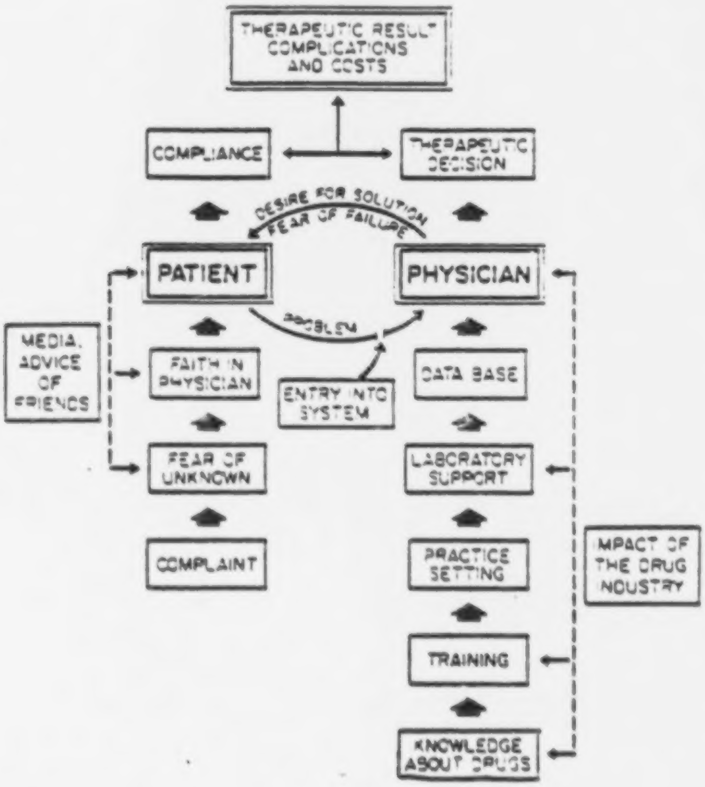

Figure 1. Outline of the elements and complex interrelationships that influence the patient and physician to use drugs.

(Data from Kunin CM. Evaluation of antibiotic usage: A comprehensive look at alternative approaches. Reviews of Infectious Diseases 1981; 3:745-753)

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Table IV-1. Multiple Constraints and Pressures That are Exerted on Physicians to Prescribe Antibiotics.

TABLE 4. Factors That Lead to Inappropriate Use of Antimicrobial Agents

Motivation of the physician to give the best treatment

Desire to provide the patient with the very best drug available without regard to outside influences such as cost; fear of failure to provide patient with the most appropriate drugs; desire to prevent infection before it may occur

Belief that if a small amount of drug will be effective, higher and more prolonged usage might be better

For example, use of high dose intravenous penicillin for pneumococcal infections rather than equally effective smaller doses of procaine penicillin

Use of multiple antimicrobial agents or "broad-spectrum agents" to "cover" unusual organisms

Often appropriate in patients with severe leukopenia, but usually used as a substitute for diagnostic judgment

Inappropriate use of resources of clinical microbiology laboratory

Failure to obtain appropriate cultures; delay in transport of specimens and receiving needed information; poor interpersonal relations with the diagnostic laboratory; lack of explanation of results of tests by the laboratory; resistance of the laboratory to use simple culture methods in wards and clinics; need for consultant for interpretation of stained specimens; availability of rapid tests such as penicillinase production, Quellung reactions, tube dilution sensitivities, serum bactericidal levels; inappropriate sensitivity testing of ineffective agents, e.g., nitrofurantoin for systemic gram-negative infection

Pressure from the patient to be treated with an antimicrobial agent

Desire to get rid of infection as soon as possible to avoid interference with life-style; concern of parents about febrile illness in their child; enhanced expectation for solution of problems by drugs; fear of the unknown

Cost and availability of x-ray film studies and diagnostic tests in relation to ready solution offered by drugs

Depends on practice setting, availability and costs of x-ray film studies and diagnostic tests, policy of third-party payors and distribution of physicians and other health care providers

Adequacy of the physician's knowledge of diagnostic and management of patients with infectious disease

Depends on extent of exposure to these disciplines in medical school and during postgraduate training; number of years since graduation, medical discipline, continuing education, self-instruction from literature, source(s) of information, experience in caring for patients with simple versus complicated infectious disease

Malpractice considerations

Have forced physicians to practice defensive medicine by ordering excessive tests and using drugs to solve anticipated problems; explain in part, overuse of oral cephalosporins in the hope that these new more expensive, but relatively safe, drugs will prevent embarrassment later on; the threat of malpractice tends to decrease usage of more toxic agents such as aminoglycoside antibiotics

Solution provided by pharmaceutical manufacturers

Take advantage of the above concerns and problems by offering often expensive and inappropriate panaceas using heavy promotion; exploitation of the "fear of failure" by the physician to help his patient and of the concept that "if it might do some good, and probably will do little harm why not try it?"

(Data from Kunin, CM. Problems in Antibiotic Usage. In: Principles and Practices of Infectious Diseases. eds. Mandell, GL, Douglas RG., Jr. and Bennett JE. 1985 John Wiley & Sons; New York pp. 305)

Table IV-2 Methods for Controlling the Use of Antibiotics in Hospitals

Table 2. Methods for control of use of antimicrobial agents in hospitals.

A. Education programs on use of antimicrobial agents
   1. Staff conferences
   2. Lectures by outside authorities
   3. Audiovisual programs
   4. Consultations with clinical pharmacists
   5. Hospital-Pharmacy Committee "newsletters"
   6. Independent sources of information (*Medical Letter, AMA Drug Evaluations*)

B. Control of contact between pharmaceutical representatives and staff physicians
   1. Registration in the pharmacy
   2. Visits to staff physicians by appointment only
   3. Policy concerning entry of salesmen to patient-care areas
   4. Restricted time and place of displays
   5. Policy on free samples, fittings
   6. Policy on sponsoring speakers, distribution

C. Hospital formulary
   1. Restriction of formulary to minimal number of agents needed for most effective therapy
   2. Elimination of duplicative agents
   3. Rules for selection of least expensive, most effective agent from a given class of agents
   4. Requirement for generic terminology for all orders and labels

D. Sensitivity tests from the diagnostic microbiology laboratory
   1. Appropriate selection of antibiotic sensitivity tests for organism and site of infection
   2. Use of generic class disks
   3. Restriction of reports on "specialized" agents unless specifically requested or indicated
   4. Use of generic terminology on laboratory report forms

E. Automatic "stop" orders for specific high-costs agents

F. Written justification for high-cost agents in cases where alternative, equally effective, less expensive, or less toxic agents may be used, e.g., oral cephalosporins, new parenteral aminoglycosides and cephalosporins, lincosamides, chloramphenicol.

G. Required consultation with infectious disease service after administration of first three doses of specific high-cost agents, e.g., aminoglycosides, parenteral cephalosporins, carbenicillin-ticarcillin, lincosamides.

H. Required approval from infectious disease consultants for release of specific agents that may alter ecology of hospital flora, e.g., amikacin, carbenicillin-ticarcillin.

I. Establishment of guidelines and audits of antimicrobial usage that permit the hospital staff to set standards of usage based on local needs and judgments, guided by independent criteria. Audit is based on voluntary compliance with these standards but requires a well-structured channel for authoritative feedback.

(Data from Kunin, CM. Evaluation of Antibiotic Usage: A Comprehensive Look at Alternative Approaches. Rev of Infect Dis 1981; 3:745-753.)

APPENDIX IV. Appropriate antibiotics for initial treatment for suspected or proven bacterial infections in patients in nursing homes.

General Guidelines: The following antibiotics are appropriate as initial treatment for suspected or proven bacterial infections at the sites noted if the specific causative agent is (a) unknown at the time of initial order, or (b) if known, it is susceptible to the antibiotic ordered and (c) if the patient is not known to be allergic to the drug ordered. The drugs, or class of drugs, are listed in alphabetical order according to the suspected or proven site of infection.

I. Urinary Tract Infections

Ampicillin Amoxicillin
Aminoglycosides
Cephalosporins
Methenamine mandelate
Nalidixic Acid
Nitrofurantoin
Sulfonamides
Trimethoprim-sulfamethoxazole
Tetracyclines

II. Upper Respiratory Infections

Ampicillin, Amoxicillin
Erythromycin
Penicillin G and V
Tetracycline
Trimethoprim-sulfamethoxazole

III. Lower Respiratory Infections

Aminoglycosides
Ampicillin, Amoxicillin
Anti-staphyloccal penicillins
(e.g., oxacillin, dicloxacillin)
Cephalosporins
Chloramphenicol (life threatening only)
Clindamycin
Erythromycin
Penicillin G or V
Tetracycline
Trimethoprim-sulfamethoxazole

IV. Skin, Subcutaneous, and Decubitus Ulcer Infections

Aminoglycosides

Anti-staphloccal penicillins
(e.g., dicloxacillin,
oxacillin)

Cephalosporins

Clindamycin

Erythromycin

V. Bone and Joint Infections

Aminoglycosides

Anti-staphyloccal penicillins
(e.g., dicloxacillin, oxacillin)

Cephalosporins

Clindamycin

VI. Genital Infections (includes specific and mixed bacterial infections plus infections due to Candida albicans, Trichomonas vaginalis and Chlamdyia trachomatis)

Ampicillin or Amoxicillin

Ketaconazole

Metronidazole

Nystatin

Tetracycline

VII. Gastroenteritis

Ampicillin

Clindamycin

Trimethoprim-sulfamethoxale

(Data from Zimmer JG, Bentley DW, Valenti WM., et al. "Antibiotic Use in Nursing Homes: A Quality Assessment," J Amer Geriatr Soc. 1985 Submitted for Publication.)

APPENDIX IV.B Recommendations for routine work-ups for suspected bacterial infections in patients in nursing homes prior to starting antibiotics

A. For any Suspected Infection:

1) History of relevant symptoms asked of the patient if adequate communication is possible, and of relevant signs and symptoms asked of facility staff, and recorded in the patient's chart.

2) Relevant physical examination, including vital signs performed and recorded.

3) Vital signs, (Temperature, pulse, respirations; B.P., if indicated) recorded every eight hour shift during the acute phase of the infection.

4) Prior to treatment obtain specimens for suspected sites of infection for gram stain and culture. Obtain peripheral WBC count and differential. If fever is > 103°F, rigors (shaking chills) are noted or hypotension is present, draw two blood cultures. Initial treatment does not have to await culture result, but should be modified, if necessary, based on the result.

B. For Suspected Specific Infections:

I. Urinary Tract Infection

Prior to treatment obtain:

1) Urinalysis on clean catch specimens from men, from specimens via straight catheterization for women, aspiration from a chronic indwelling catheter or from frequently observed drainage from a sterile condom collecting system if required.

2) Urine culture, colony count and sensitivities on a portion of the same specimen noted above.

II. Upper Respiratory Infection:

Prior to treatment obtain:

1) Culture of throat exudate for Group A Stretococcus.
2) Culture and sensitivities of purulent sinus or ear drainage, if present

III. Lower Respiratory Infection

Prior to treatment obtain:

1) Culture and gram stain of best available secretation from lower tract. Gram stain to include "scoring" for squamous epithelial cells, i.e., <10, 10-25 or >25 per lowpower field (100x magnification).
2) Chest X ray, especially if pneumonia is suspected but not supported on initial physical examination.

IV. Skin, Subcutaneous, and Decubitus Ulcer Infections

Prior to treatment obtain:

1) Culture and sensitivities of any purulent drainage, or aspirate of abscess if present.

V. Bone or Joint Infections (e.g., osteomyelitis, septic joint)

Prior to treatment obtain:

1) Culture and sensitivities of purulent drainage, aspiration or biopsy
2) X ray of affected bone or joint

VI. Genital Infections (vaginitis, cervicitis, endometritis, or epididymitis).

Prior to treatment obtain:

1) Microscopic examination of exudate to rule out Trichomonas or Candida.
2) Culture and sensitivities of exudate.

VII. Gastroenteritis

Prior to treatment obtain:

1) Microscopic examination of stool for fecal leukocytes.
2) Culture of stool for bacterial pathogens.

(Data from Zimmer JG, Bentley DW, Valenti WM, et al. "Antibiotic Use in Nursing Homes: A Quality Assessment," J Amer Geriatr Soc. 1985 Submitted for Publication).

APPENDIX IV-C Minimum criteria for starting antibiotics in patients in nursing homes with suspected or proven infections.

Urinary Tract Infection

A. Laboratory Results Available within 14 days of the drug order

1) Urinalysis demonstrates:

a) bacteria on gram stain of unspun urine OR

b) WBCs $\geq$ 10 hpf OR

c) 'marked' pyuria, OR

d) 'loaded' with WBCs, OR

2) Urine culture results demonstrate:

a) $\geq$ 100,000 organisms per ml if no indwelling catheter present

b) $\geq$ 10,000 organisms per ml if an indwelling catheter present plus

1) fever of $\geq$ 100°F on the day of the drug order, OR

2) costovertebral or suprapubic tenderness, OR

3) gross hematuria, OR

3) Blood Culture demonstrates a urinary tract pathogen, e.g. *E. coli*, *Klebsiella* species, *Proteus* species, *Ps. aeruginosa* etc. and no other suspicious site of infection

B. No Laboratory Results Available

1) Fever of 100°F on the day of drug order plus

a) gross hematuria or pyuria as noted in IA, OR

b) costovertebral or suprapubic tenderness, OR

c) urinary frequency of recent onset, OR

d) burning or pain on urination, OR

2) No fever, but any two of the four symptoms listed in B1

II. Upper Respiratory Infection

A. Laboratory Results Available

1) Positive culture of (throat exudate, nasal or ear purulent drainage for URI pathogen, e.g., GPA Streptococcus (Throat), *S. aureus, H. influenzae, S. pneumoniae* (nasal or ear) alone

2) Positive sinus X ray alone

B. Laboratory Results Not Available

1) Throat exudate alone

2) Purulent sinus drainage alone, or sinus tenderness or pain alone

3) Purulent ear drainage alone

III. Lower Respiratory Infection

A. Laboratory Results Available

1) New infiltrate on chest X ray compatible with pneumonia, pneumonitis, inflammation, PLUS

   a) Culture of best available lower respiratory tract secretion demonstrates lower respiratory pathogen(s), OR normal throat flora, OR

   b) Fever ≥ 100°F on day of drug order, OR

   c) Peripheral WBC count > 10,000 per mm^3, OR

   d) Peripheral WBC count ≤ 10,000 per mm^3 with a left shift, OR

2) Culture of best available lower respiratory tract secretion demonstrates acid-fast bacteria on smear or culture yields *M. tuberculosis*, PLUS infiltrate on chest X ray compatible with tuberculosis.

B. No Laboratory Results Available

1) New cough and purulent respiratory secretions PLUS

   a) Fever of 100°F or more on day of drug order, OR

b) Tachypnea (26 respirations per minute or more), OR

c) One physical sign of pneumonia (e.g., rales, dullness to percussion), OR

2) Fever≥100° on the day of the drug order, PLUS

a) tachypnea (26 respirations per minute or more), OR

b) one physical sign of pneumonia (e.g., rales, dullness to percussion), OR

3) New cough with increased purulent respiratory secretions (only if patient has COPD).

IV. Skin, Subcutaneous and Decubitus Ulcer Infections

A. Laboratory Results Available

1) Culture of purulent drainage or aspirate of abscess demonstrating appropriate pathogen

B. Laboratory Results Not Available

1) Purulent draingage from open skin and soft tissue infections (e.g., decubiti or wounds); OR

2) Aspirated pus from closed skin and soft tissue infections (e.g., cellulitis, abscess, etc.), OR

3) Red, warm, tender or swollen site

V. Bone or Joint Infections (e.g., osteomyelitis, septic joint)

A. Laboratory Results Available

1) Culture and sensivities of purulent drainage or aspiration, OR

2) X ray demonstrates new findings compatible with infection

B. Laboratory Results Not Available

1) Purulent drainage or aspirated pus alone

(Data from Zimmer JG, Bentley DW, Valenti WM, et al. "Antibiotic Use in Nursing Homes: A Quality Assessment," J Amer Geriatr Soc . 1985 Submitteu for Publication).

Appendix H

SPECIAL PROJECT: Withholding/Prescribing Antibiotics in a Nursing Home

Peter Mott, M.D. and William Barker, M.D.

One hundred and ten residents in a skilled nursing home, cared for by a group practice of four internists over a period of seven years, were classified according to how aggressively they should be managed in the event of life-threatening acute illness. Based on informal discussions between the resident, his/her family, the nursing staff and attending physician, each individual was placed in one of four classes as follows:

1. To receive full, unrestricted medical intervention.
2. Intermediate - probably full intervention.
3. Comfort care/intermediate - primarily restrict to comfort and supportive care, possibly provide agressive medical intervention for life-threatening episode.
4. Comfort care and attention to basic medical needs only.

Over the seven year period about one fourth of the residents were reassigned to a different care category as their condition changed, invariably in a deteriorating direction. There was no formal system for documenting the care categories, but residents' charts carried a simple code to indicate category and serve as a guide to the attending physician and nursing staff.

Resident Characteristics

Table 1 presents selected demographic and diagnostic characteristics of the residents in the respective care categories. Those in the comfort care categories (3 and 4) were more likely to have a diagnosis of either terminal cancer or dementia. While two thirds of persons in categories 1-3 had multiple major chronic diseases, approximately two thirds in category 4 had only one diagnosis, usually dementia.

Table 2 compares mental and functional status measurements among the four care categories. On virtually all of these parameters, there was a progressively greater degree of dependence or failing function on moving across the continuum from category 1 to 4.

Infections

Tables 3, 4 and 5 summarizes the occurrence and treatment of pulmonary, urinary tract and skin/decubitus infections, respectively, among persons in each of the care categories.

a) Pulmonary Infection (Table 3)

Rates of acute pulmonary infection were lowest among those in category 1 (38 per 1000 resident-months) and highest for those in category 4 (75 per 1000 patient-months). On the other hand, 28 of 58 (48%) of the former were transferred to acute hospital for medical care while only 3 of 23 (13%) of the latter were transferred. Furthermore, among the 30 episodes of acute pulmonary infection among category 1 residents which were managed in the nursing home all but one received a course of specific antibiotic treatment, while this was the case for only 10 (50%) episodes of acute pulmonary infection among category 4 patients which were managed in the nursing home.

b) Urinary Tract Infection (Table 4)

Rates of acute UTI were, as with pulmonary infection, highest among persons in Category 4. Again there was a striking contrast in frequency with which UTI was managed by transferring to acute hospital, according to care category: 40% of UTIs in category 1, 28% in category 2, none in category 4. When UTI was managed within the nursing home, all of 27 episodes among category 1 residents were given a specific course of antibiotics, while such therapy was withheld in 5 of 13 (38%) of episodes among category 4 residents.

c) Skin/Decubitus Ulcer Infections (Table 5)

Rates of medically-attended skin and/or decubitus ulcer infection were slightly higher among category 1 and 2 patients. None of these infections led to hospitalization. While 100% of episodes involving patients in categories 1,2,3 were treated with antibiotics, only 57% (4 of 7) of such infections among category 4 patients were treated.

d) Mortality (Table 6)

Nineteen percent (28 of 147) of all pulmonary infections and 9% (8 of 92) of all urinary tract infections had fatal outcomes.

All pulmonary infections with fatal outcome among category 1 and 2 patients represented episodes for which antibiotics were administered. None of the small number of untreated episodes of pulmonary infection among these patients were fatal. The converse pattern pertained among those in categories 3 and 4: all deaths resulted from untreated episodes, while no deaths resulted from treated episodes. Interestingly, the overall case fatality rates for pulmonary infections were only slightly greater among persons in categories 3 and 4 (29% and 22%, respectively) than among persons in categories 1 and 2 (19% and 15%).

These data suggest that a certain proportion (roughly 20-25%) of all pulmonary infections among nursing home patients are destined to lead to a fatal outcome, with or without treatment. While the data in the study are not sufficiently detailed to draw further conclusions, it is reasonable to speculate that most of the fatal pulmonary infections occurred at points when the patients were particularly weakened and vulnerable from underlying chronic disability.

Summary/Discussion

In this case study, the subgroup of nursing home patients assigned to comfort care, as opposed to those for whom full care wrap deemed appropriate, were both the most disabled, by a series of measures (Table 2) and the most likely to experience episodes of pulmonary infection and urinary tract infection. (Table 3 & 4). The intent to withhold agressive medical treatment for these infections and other potential life-threatening illnesses among the comfort care groups was indeed fulfilled as they were transferred to hospital and treated with antibiotics much less often than was the case for those assigned to the full intervention groups. Despite the differences in treatment patterns, the case-fatality rates for pulmonary infection did not appear to differ significantly between the several subgroups of nursing home residents. This observation suggests that most instances in which antibiotics were withheld were destined for a terminal outcome with or without antibiotics.

Fatal outcomes were too few in any care group of residents. For UTI and were non-existent for skin/decubitus infection in this population; hence analyses of the effect of withholding antibiotics in these infections are not possible.

Table 1

Demographic and Diagnostic Characteristics of Nursing Home Residents By Medical Care Categories

Characteristics(a)	Medical Care Categories(b)									
	1		2		3		4		Total	
	N	%	N	%	N	%	N	%	N	%
Number(c)	62		40		19		15		136	
Age (mean)	82		83		79		84			
Sex male	17	27%	8	20%	5	26%	3	20%	33	24%
female	45	73	32	80	14	74	12	80	103	76
Diagnoses										
arteriosclerotic heart disease	26	42%	17	43%	6	32%	3	20%	52	38%
stroke/T.I.A.	17	27	6	15	2	11	5	33	30	22
other cardiovascular	10	16	5	13	0	0	2	13	17	13
respiratory diseases	4	6	3	8	1	5	1	6	9	7
diabetes	13	21	7	20	3	16	0	0	24	18
cancer	4	6	1	3	2	11	2	13	9	7
dementia	28	45	29	73	18	95	13	87	85	63
other neurologic	7	11	4	10	2	11	0	0	13	10
psychiatric	3	5	0	0	0	0	0	0	3	2
other	18	29	9	23	3	16	0	0	30	22
Multiple Diagnoses										
1	20	32	12	30	6	32	9	60	47	35
2-3	35	56	26	65	13	68	5	33	79	58
3	7	11	2	5	0	0	1	6	10	7

Footnotes

a. Patient characteristics existing at the time of assignments to patient care category

b. Care categories: (1) unrestricted care, (2) intermediate, (3) comfort/intermediate, (4) comfort care only

c. Number of residents who at any time were assigned to each care category (i.e., not the total number of people).

Table 2

Mental Status and Functional Capabilities of Nursing Home Residents
By Medical Care Categories

Characteristics	1		2		3		4		Total	
	N	%	N	%	N	%	N	%		
# Residents	62		40		19		15			
Mental Status(a)										
normal	44	71%	13	33%	0	0%	2	13%	59	43%
slight abnormalities	13	21	15	38	2	11	0	0	30	22
moderate-severe	5	8	12	30	10	53	6	40	33	24
no communication	0	0	0	0	7	37	7	47	14	10
A.D.L. Functions(b)										
Ambulating										
no help needed	16	26%	7	18	2	13	0	0	25	20
some help needed	30	50	16	42	6	38	2	17	54	43
total help needed	14	23	15	39	8	50	10	83	47	37
Urination										
no(minimal) help needed	29	48	9	24	2	13	0	0	40	32
some help needed	14	23	7	19	3	19	1	8	25	20
total help needed	17	28	21	57	11	69	11	92	60	48
Dressing										
no (minimal) help needed	14	23	5	13	1	6	0	0	20	16
needed help	46	77	33	87	15	94	12	100	106	84
Feeding										
no/minimal help needed	42	70	17	45	5	33	0	0	64	52
needed help	18	30	21	55	10	67	11	100	60	48
Bathing										
no/minimal help needed	11	18	1	3	0	0	0	0	12	10
some help needed	31	52	21	55	9	56	5	42	66	52
total help needed	18	30	16	42	7	44	7	58	48	38

Footnotes:

a. Mental status as judged by the physician in annual physical exams and regular visits throughout the period of care
b. Assessment activities of daily living by utilization review at start of each period of care

Table 3

Occurrence and Treatment of Acute Pulmonary Infection* Among Nursing Home Residents by Medical Care Category

	Care Category				
	1	2	3	4	Total
# Residents	62	40	19	15	136
Months of Care	1541	990	333	308	3172
# Pulmonary Infections	58	52	14	23	147
Per 1000 mos.	38	53	42	75	46
Disposition					
Hospital	28(48%)	13(25%)	1(7%)	3(13%)	45(31%)
Nursing Home	30(52%)	39(75%)	13(93%)	20(87%)	102(69%)
Specific Treatment in Nursing Home					
Yes	29(97%)	35(90%)	7(54%)	10(50%)	81(79%)
No	1(3%)	4(10%)	6(46%)	10(50%)	21(21%)
Total Episodes Treated**	57(98%)	48(92%)	8(57%)	13(56%)	126

[*] Includes pneumonia, aspiration pneumonia and acute bronchitis.

[**] Sum of episodes treated in hospital or receiving specific treatment in nursing home. (underlined)

Table 4

Occurrence and Treatment of Urinary Tract Infection (UTI) Among Nursing Home Residents by Medical Care Category

	Care Category				
	1	2	3	4	Total
# Residents	62	40	19	15	136
Months of Care	1541	990	333	308	3172
# UTI	45	25	9	13	92
Per 1000 mos.	29	25	27	42	29
Disposition					
Hospital	18(40%)	7(28%)	1(11%)	0	26(28%)
Nursing Home	27(60%)	18(78%)	8(89%)	13(100%)	66(72%)
Specific Treatment in Nursing Home					
Yes	27(100%)	17(94%)	7(87%)	8(62%)	59(89%)
No	0	1(6%)	1(13%)	5(38%)	7(11%)
Total Episodes Treated*	45(100%)	24(96%)	8(89%)	8(62%)	85(92%)

*Sum of episodes treated in hospital or in nursing home (underlined).

Table 5

Occurrence and Treatment of Skin/Decubitus Ulcer Infections Among Nursing Home Residents by Medical Care Category

	Care Category				
	1	2	3	4	Total
# Residents	62	40	19	15	136
Months of Care	1541	990	333	308	3172
# Skin/DU Infection	11	10	3	7	31
Per 1000 mos.	7	10	9	23	10
Disposition					
Hospital	0	0	0	0	0
Nursing Home	11(100%)	10(100%)	3(100%)	7(100%)	31(100%)
Specific Treatment in Nursing Home					
Yes	11(100%)	10(100%)	3(100%)	4(57%)	28(90%)
No	0	0	0	3(43%)	3(10%)
Total Episodes Treated*	11(100%)	10(100%)	3(100%)	4(57%)	28(90%)

*Sum of episodes treated in hospital or receiving specific treatment in nursing home.

Table 6

Mortality from Pulmonary and Urinary Tract Infections Among Nursing Home Residents by Medical Care Category and Treatment Decisions

	Care Category				
	1	2	3	4	Total
Pulmonary Infection					
Total Treated*	57	48	8	13	126
Deaths	11	8	0	0	19
Case-Fatality Rate	19%	16%	-	-	15%
Total Untreated	1	4	6	10	21
Deaths	0	0	4	5	9
Case-Fatality Rate	-	-	66%	50%	43%
Total	58	52	14	23	147
Deaths	11	8	4	5	28
Case-Fatality Rate	19%	15%	29%	22%	19%
Urinary Tract Infection					
Total Treated*	45	24	8	8	85
Deaths	3	2	1	0	6
Case-Fatality Rate	7%	8%	12%	-	7%
Total Untreated	0	1	1	5	7
Deaths	-	0	0	2	2
Case-Fatality Rate	-	-	-	40%	28%
Total	45	25	9	13	92
Deaths	3	2	1	2	8
Case-Fatality Rate	7%	8%	11%	15%	9%

*Sum of episodes treated in hospital or given specific treatment in nursing home. (See tables 3 and 4).

PSYCHOSOCIAL VARIABLES AS PREDICTORS OF TREATMENT CHOICE IN ELDERLY NURSING HOME RESIDENTS

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One hundred and seventy-four elderly residents of three nursing homes in the Rochester, N.Y. area were surveyed for evidence of febrile episodes and the concomitant antibiotic treatment decisions during a one year period in 1984. These data were then analyzed with information regarding the psychological functioning, quality of life, social support, and functional ability of these elderly persons. The psychosocial data were gathered as part of an ongoing study of the Immune Response of the Elderly to Pneumococcal Vaccine (R01 AG03795), Dr. David Bentley, Assoc. Professor of Medicine, Principle Investigator.

It is unclear if and how the psychosocial characteristics of the patient influence the caregivers' attitudes towards that patient and affect the ultimate treatment decision. The purpose of this study is therefore to provide information to address the following questions: In those patients experiencing a febrile episode,

1. Is there a difference in the patient's psychological state between those treated and those not treated with antibiotics? Specific measures to include self-reported level of mental health, change in level of mental health over the previous five years, and level life satisfaction.
2. Is there a difference in the level of social support between those treated and those not treated with antibiotics? Specific measures to include the presence of family and friends who visit regularly and engage in activities with the patient.

3. Is there a difference in the demographic characteristics and pre-infection functional ability of those treated and those not treated with antibiotics? Specific measures to include level of education, previous occupation, and marital status.

The operational definition of fever utilized in this study is identical to that used by Brown and Thompson (1979); ie. two temperatures of 101 to 101.9^{0}F within a 24-hour period of one temperature of $>102^{0}$F. Antibiotic treatment was defined as the initiation of oral, parenteral, or intravenous antibiotics upon order from a physician or nurse-practitioner. Propriety of the dose, medication, route of administration, and duration of the treatment regimen were not assessed; emphasis was placed upon the treatment decision alone. It has been assumed for this study that physicians and nurses will not treat life-threatening illness actively in elderly nursing home residents under certain circumstances (Brown & Thompson) and the process of arriving at a treatment decision is not random and reflects characteristics of the patient, family, physician, nursing staff, and the facility. This study examines the patient characteristics.

METHODS

Population and Fevers Studied

Three extended-care facilities within the Rochester, N.Y. area were utilized to conduct a retrospective chart review of 174 residents already enrolled ~~into~~ a pneumococcal vaccine study in order to assess episodes of fever during a twelve-month period. Confidentiality of the records and institutions was assured and the Committee for the Investigation of Human Subjects of the University or Rochester approved extension of the original pneumococcal vaccine study. The charts were reviewed by the same research nurse in all three facilities. Thus, 174 charts were reviewed for a one year period from time of admission into the vaccine study until 12 months later, death, or discharge from the facility for the occurence of two oral or rectal temperatures of 101 to 101.9°F within a 24-hour period or any single temperature of 102°F or greater. Brown and Thompson considered these temperatures as serious rather than inconsequential, and could be construed to be life-threatening when occurring in elderly nursing home residents.

To facilitate statistical analyses, Chi-square tests (SPSSx) were utilized to identify factors that most separated the patients with fevers who were treated from those not treated. The P Values reported in the text and tables are for the standard chi-square test for two-way tables, uncorrected.

One or more febrile episodes were observed in 91 (52%) of the patients. Forty-nine patients experienced 1 episode of fever, 21 experienced 2 episodes, 11 experienced three episodes, 4 experienced four episodes, 5 experienced five episodes, and one patient experienced six episodes of fever.

In the facilities utilized for the study, temperatures of residents were not routinely measured after admission, and these measurements usually reflected the nursing staff's suspicion that the patient's status had somehow changed. Oral and rectal temperatures are reported in this study.

Characteristics of the Patients

Demog~~ra~~phic characteristics were abstracted from the charts of the 174 residents and include age, sex, race, marital status, level of care required, number of pre-infection diseases and ambulatory status. These characteristics are summarized in Table 1.

Table 2 summarizes the extent and nature of those residents with treatment preferences noted in the chart, kardex, or doctor's order sheet. Although comfort care is not defined specifically by any of the participating institutions, it is generally construed to mean that only treatment which will ultimately enhance the comfort and quality of life of the patient are to be undertaken. Also illustrated in Table 2 is the origin of the treatment preference when it was stated in the patient's medical record. In no case was there disagreement noted between patients, families, and physicians, leading to the conclusion that only fully-agreed upon treatment decisions are entered in the patient's chart.

Infections

The remainder of this study concerns only those 91 patients experiencing one or more episodes of fever. Table 3 summarizes the occurrence of the provisional diagnoses of pneumonia, upper respiratory tract infection (URI), urinary tract infection (UTI), and other infections in those patients with fever. UTI's comprised the most common source of infection in this study with 45% of those with fever receiving this provisional diagnosis. Of the 91 infections noted in this study, 74 (81%) were treated with antibiotics while 17 (19%) received no antibiotic treatment. Symptoms were controlled with aspirin or tylenol in 57 (63%) of the patients, cough medicine in 8 (9%) of patients, and intravenous therapy in 15 (16%) of patients. In addition, 20 patients (21%) received additional comfort measures such as nasal oxygen, warm soaks, or topical antibiotics.

Table 4 illustrates the outcome of these febrile events. As noted, most of the infections were managed in the nursing home and resulted in recovery (71%). Also presented is the outcome by treatment, noting that of the antibiotic-treated patients (N=74), 68 (92%) recovered while 6 died. Of the untreated patients (N=17), 15 (88%) recovered and 2 died, resulting in no significant differences (P=.168) between the treated and untreated groups. These findings fail to replicate Brown and Thompson's in which they noted a significant difference (P<0.001) between the 59% who died of fever while not-treated and the 9% who died after treatment.

To answer research question #1, the psychological state of the patient was examined to identify any differences between those treated with antibiotics and those not treated. This information is presented in Table 5. As noted there were no significant differences identified when mental health and life satisfaction measures were examined.

The second research question addressed any possible differrences between levels of social support between the two groups. The social support data are presented in Table 6. Again, there are no significant differences between the social support measures and the antibiotic treatment decision.

The data for the final research question are presented in Tables 7 and 8. Again there are no significant differences noted on the demographic variables (Table 7), including marital status which was found to be a significant predictor of treatment by Brown & Thompson. Even age was not significantly related to the treatment decision, (P=.124), however more patients over 80 were not treated with antibiotics. Table 8 presents no significant differences between the treated and not treated when functional ability, self-rated health, and number of pre-infection illnesses and medications are examined. However, when the presence of individual diseases was examined including arthritis, impaired sight/hearing, dementia, emphysema, hypertension, coronary artery disease, ulcer/stomach disorders, liver dysfunction, urinary/kidney dysfunction, cancer, effects of stroke, and psychiatric disorders, all were found to be non-significantly related to the treatment decision except for the diagnosis of dementia (P=.05). The demented person was less likely to undergo antibiotic treatment. Of the 35 persons with dementia who experienced a febrile episode, 25 were treated with antibiotics for febrile events and 10 were not treated.

Further Findings

The entire sample (N=174) was then dichotomized into those under 80 and those over 80 in order to examine the relationship between age and treatment preference. Age was significantly related to the placement of a notation on the chart designating a treatment preference (P=.003) with those over 80 more likely to have such a notation. When the nature of the treatment preference was examined, the 80+ group was more likely to request no resuscitation (P=.01) and comfort care (P=.01). When the origin of the treatment preference was examined, there was no significant relationship between physician and family preference and age, however, the older the patient, the more likely the preference originated with the patient (P=.01). Also significantly related to advanced age was the tendency to have designated that treatment preference within the last year with the over 80 signficantly more likely to have changed their status from full treatment to either comfort care only or DNR (P=.006).

There was no signficant relationship between age and the patient having been resuscitated or receiving nutritional support, including nasogastric tube, supplemental oral feedings, and gastrostomy tube.

There was further no significant relationship between treatment decision and size of the facility, facility and age of the patient, or provision of supplemental comfort measures by age (oxygen, aspirin, cough meds, etc.) ~~or~~ level of care (SNF vrs. HRF).

SUMMARY/DISCUSSION

In this study the relationship between psychosocial variables and antibiotic treatment decision for febrile episodes was examined. There was no significant relationship found between the patient's psychological state, levels of social support, or demographic or functional characteristics. These findings replicate those of Brown and Thompson with the exception of marital status which was a significant predictor of treatment in their study. Perhaps the unmarried in our study had living adult children or involved friends who were more likely to intervene than the Brown and Thompson population. Despite the small size of this sample, the failure to replicate this finding regarding the relationship between marital status and treatment decision indicates the need for further study.

There was also no significant difference in mortality patterns by treatment decision. This may reflect that fact that propriety and efficacy of the treatment decision were not reviewed within this paper. It may be that certain patients are prescribed oral, sub-therapeutic doses of antibiotics in order to ease symptoms and allow the staff, family, and physician to feel that indeed something is being done (see Hilfiker, 1983).

The presence of dementia was found to be the only disease significantly related to the antibiotic treatment decision, indicating that this diagnosis may indeed involve certain difficulties involved with the diagnosis, treatment, possible transfer to an acute care facility, and other burdens to the patient. It appears that quality of life assessments impact upon the ultimate treatment decision. As the demented patient is not likely to have made his/her own treatment decision (especially since the onset of t~~he~~ dementia) it must be assumed that caregivers and families have discussed the benefits/burdens involved with antibiotic treatment. In no case was there disagreement noted on the chart, leading one to believe if disagreement is present among or between families and caregivers, no notation at all is made, and treatment decisions are handled individually as the need arises.

It is however, of interest to note that the old-old (80+) are more likely to have a treatment preference noted on their medical record, and the origin of the preference is more likely to be from the patient themselves with advanced age. It is somewhat reassuring to note that families and physicians do not use age as the sole criterion upon which to base decisions regarding treatment preference.

Finally, there was no significant difference in treatment patterns between the three institutions utilized for this study. One is a large county facility, and two are private non-profit nursing homes with one facility representing a more affluent patient population than the other. This may be due to the fact that many of the physicians and nurse-practitioners attending the patients in these facilities are affiliated with the University of Rochester and may in fact attend conferences, consult, and frequently interact with each other on a professional basis. Perhaps the differences found by Brown & Thompson between size of facility and treatment decisions related to differences resulting from individual preferences among physicians and other providers of care.

REFERENCES

Brown N.K. & Thompson, D.J. (1979) Nontreatment of fever in extended-care facilities. New England Jounral of Medicine, 300, No. 22, 1246-1250.

Hilfiker D. (1983) Sounding board. Allowing the debilitated to die. New England Journal of Medicine, 308, No. 12, 716-719.

TABLE 1

Demographic Characteristics of Nursing Home Residents

N= 174

AGE mean=80	65-79 87 (50%)	80+ 87 (50%)		
SEX	Male 75 (43%)	Female 99 (57%)		
RACE	Black 14 (8%)	White 160 (92%)		
MARITAL STATUS	Single 34 (20%)	Married 30 (17%)	Widowed 88 (51%)	Divorced 22 (13%)
LEVEL OF CARE	HRF 93 (53%)	SNF 81 (47%)		
AMBULATORY STATUS	Independent 52 (30%)	W/Assistance 77 (44%)	Bed-fast 45 (26%)	

Medical Diagnoses of Nursing Home Residents

Diagnosis	Present	Absent
Arthritis	58 (33%)	116 (67%)
Impaired Senses	43 (25%)	131 (75%)
Dementia	67 (39%)	107 (61%)
Emphysema	35 (20%)	139 (80%)
Cardiovascular	99 (57%)	75 (43%)
Diabetes	31 (18%)	143 (82%)
Urinary Tract D/O	33 (19%)	141 (81%)
Cancer	10 (6%)	164 (94%)
Stroke Effects	55 (32%)	119 (68%)
Psychiatric D/O	31 (18%)	143 (82%)

TABLE 2

Presence, Nature & Origin of Treatment Preference

TREATMENT PREFERENCE NOTED (N=174)	YES	NO
	33 (19%)	141 (81%)

NATURE OF PREFERENCE (N=33)		
DNR	18 (55%)	15 (45%)
Comfort Care	15 (45%)	18 (55%)

ORIGIN OF PREFERENCE	Patient	Family	Physician
N=33 *	11 (33%)	19 (58%)	29 (88%)

DISAGREEMENT NOTED	YES	NO
N=33	0 (0%)	33 (100%)

CHANGE IN PREFERENCE DURING LAST YEAR **	YES	NO
	22 (13%)	152 (87%)

Footnotes

* Categories are not mutually exclusive. Preference may have originated from more than one person.

** Change was always from full-treatment to DNR or Comfort Care.

TABLE 3

PROVISIONAL DIAGNOSES OF THOSE PATIENTS WITH FEVER

N=91

DIAGNOSIS	YES	NO
Pneumonia	14 (15%)	77 (85%)
Upper Respiratory	37 (41%)	54 (59%)
Urinary Tract Inf.	41 (45%)	50 (55%)
Other Infections*	40 (44%)	51 (56%)

*Includes other infectious diseases and combinations of URI, Pneumonia, and UTI.

TABLE 4

OUTCOME OF FEBRILE EVENTS (N=91)

Infection managed in	Nursing Home	Hospital	Total N
Recovery	65 (71%)	18 (20%)	83(91%)
Death	5 (6%)	3 (3%)	8 (9%)

OUTCOME BY TREATMENT

	Treatment	No Treatment	
Recovery	68 (92%)	15 (88%)	83 (91%)
Death	6 (8%)	2 (12%)	8 (9%)

TABLE 5

PSYCHOLOGICAL CHARACTERISTICS OF RESIDENTS BY TREATMENT DECISIONS

	TREATED	NOT TREATED	P<.05*
EMOTIONAL HEALTH			NS
POOR	7	1	
FAIR	14	2	
GOOD	28	6	
MENTAL HEALTH NOW COMPARED TO 5 YRS AGO			NS
WORSE	15	4	
SAME	22	5	
BETTER	12	0	
LIFE SATISFACTION			NS
POOR	3	0	
FAIR	13	2	
GOOD	32	6	

* Chi-Square test for 2-way tables, uncorrected.

TABLE 6
SOCIAL SUPPORT MEASURES BY TREATMENT DECISION

Treated	Yes	No	P<.05*
Patient has living family	72	16	NS
Patient sees fam/friends often	19	5	NS
Patient has someone to trust/ confide in	45	8	NS
Patient can get help from family if needed	42	6	NS
* Visits from friends/family in past week			NS
None	11	1	
One	18	2	
2 - 6	11	5	
Every day	11	0	

* Chi-Square test for 2-way tables, uncorrected

TABLE 7

DEMOGRAPHIC VARIABLES BY TREATMENT DECISION

Treatment	Yes	No	P<.05*
Level of Education			NS
Grammar School	42	5	
High School	14	4	
College	16	3	
Previous Occupation			NS
Housewife	14	1	
Semi-skilled laborer	8	3	
Unskilled laborer	23	5	
Clerical, sales, service	6	1	
Professional, managerial	11	3	
Other	10	3	
Marital Status			NS
Single	20	2	
Married	11	2	
Widowed	32	13	
Divorced/Separated	11	0	
Age			NS
Under 80	37	5	
Over 80	37	12	

*Chi-Square test for 2-way tables, uncorrected.

TABLE 8

FUNCTIONAL ABILITY VARIABLES BY TREATMENT DECISION

Treatment	Yes	No	$P<.05$*
Use of telephone			NS
No	34	8	
Yes with help	11	4	
Yes, alone	27	5	
Continent of urine/feces			NS
No	29	6	
Yes	45	11	
Self-Rated physical health			NS
Poor	3	2	
Fair	36	7	
Good	27	5	
Excellent	1	0	
Number of Pre-Infection Illnesses			NS
1 - 2	5	3	
3 - 5	45	11	
6 - 8	24	3	
Number of Pre-Infection Medications			NS
0-2	16	4	
3-5	46	11	
6-7	12	2	

*Chi-Square test for 2-way tables, uncorrected.

Form #1
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Aug 12, 1985

OTA SUPPLEMENTAL STUDY OF IREP
PSYCHOSOCIAL DETERMINANTS OF ANTIBIOTIC TREATMENT DECISIONS

To be completed on all IREP study volunteers:

IDENTIFICATION NUMBER: ___ ___-___ ___ ___ ___

NAME:

______________________, ______________________, ______________
Last, First, M.Init.

DOES THIS PATIENT HAVE LIVING FAMILY MEMBERS
1 NO
2 YES ___

IS THERE A NOTATION ON THE CHART REGARDING TREATMENT PREFERENCE?

1 NO
2 YES ___

IF YES, WHERE DOES THE NOTATION APPEAR?

1 KARDEX
2 PHYSICIAN'S ORDER SHEET
3 PROGRESS NOTES
4 OTHER (PLEASE SPECIFY) ______________________ ___

IF YES, TREATMENT PREFERENCE NOTED?

1 DO NOT RESUSCITATE
2 COMFORT CARE ONLY
3 OTHER (PLEASE SPECIFY) ______________________ ___

IF YES, ORIGIN OF PREFERENCE

1 PATIENT PREFERENCE
2 FAMILY PREFERENCE
3 PHYSICIAN PREFERENCE
4 OTHER (PLEASE SPECIFY) ______________________ ___

FOR THOSE WITH KNOWN PREFERENCE, IS THERE DISAGREEMENT NOTED?

1 NO
2 YES ___

HAS THERE BEEN A CHANGE IN TREATMENT PREFERENCE?

1 NO
2 YES ____

HAS THE PATIENT BEEN RESUSCITATED?

1 NO
2 YES ____

IS/HAS THE PATIENT RECEIVED NUTRITIONAL SUPPORT?

1 NO
2 YES ____

IF YES, NOTE FORM OF THAT SUPPORT

1 NASOGASTRIC TUBE
2 GASTROSTOMY TUBE
3 INTRAVENOUS FLUIDS
4 SUPPLEMENTAL HIGH CALORIC FEEDINGS ____

DID THIS PATIENT SUPPLY HIS/HER OWN CONSENT FOR THE STUDY?
1 NO
2 YES ____

DID THIS PATIENT HAVE A CONFIRMED OR SUSPECTED INFECTION?

1 NO
2 YES ____

IF YES PLEASE NOTE NUMBER OF EVENTS ____

DID THIS PATIENT HAVE A FEBRILE EVENT? (FOR THIS STUDY, THIS IS DEFINED A THE PRESENCE OF TWO ORAL OR RECTAL TEMPERATURES OF 38.33 TO 38.83 C (101 TO 101.9 F) WITHIN A 24 HOUR PERIOD OR ANY SINGLE TEMEPRATURE OF 38.88 C (102 F) OR GREATER).

1 NO
2 YES PLEASE NOTE HIGHEST TEMPERATURE ____________ ____

DID PATIENT UNDERGO A DIAGNOSTIC WORK UP?

1 NO
2 YES FOR HOW MANY EVENTS ________ ____

IF YES, NATURE OF THIS WORK-UP:

1 CHEST X-RAY
2 URINE C&S
3 SPUTUM
4 BLOOD C&S
5 OTHER (PLEASE SPECIFY) ________________ ____

PROVISIONAL DIAGNOSIS:

1 PNEUMONIA
2 URI
3 UTI
4 OTHER (PLEASE SPECIFY) ____________________ ___

WAS PATIENT TREATED WITH ANTIBIOTICS?

1 NO
2 YES ___

IF YES, STATE NUMBER OF OCCASIONS

1 ALL
2 OTHER (PLEASE SPECIFY) ____________________ ___

DID PATIENT RECEIVE OTHER TREATMENTS?

1 ASA/TYLENOL
2 COUGH MEDICINE
3 IV's
4 OTHER (PLEASE SPECIFY) ____________________ ___

OUTCOME OF FEBRILE EVENTS (CHECK ALL THAT APPLY)

1 PATIENT RECOVERY
2 PATIENT DEATH
3 HOSPITALIZATION
4 INCREASE IN LEVEL OF CARE ___

COMPLETED BY: ____________________

CHECKED BY: ____________________

TECHNOLOGY ASSESSMENT
ON
FUTURE DEVELOPMENTS IN LIFE SUSTAINING TECHNOLOGIES FOR ELDERLY

For Office of Technology Assessment,
Congress of the United States

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TASK I: ADVANCES IN RENAL DIALYSIS TECHNOLOGY

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TASK I: Advances in Renal Dialysis Technology

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II. Present Status
  2-A Artificial Kidney
   Miniaturization
   Absorbent
   Continuous Ambulatory Peritoneal Dialysis (CAPD)
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   Continuous Arteriovenous Hemofiltration (CAVD)
  2-B Plasmapheresis
   Absorbent
   Membrane filtration
III. Strategy

I. OVERVIEW

In order to sustain or provide an improved quality of life for the elderly, various types of artificial organ technologies are available and being successfully applied. One technology available is hemodialysis. Originally, the patient population on dialysis was relatively young; however, the life sustaining capability of hemodialysis has been such that the current average age of the dialysis patient is now considerably higher and is increasing yearly. The mean age of patients beginning chronic dialysis is rapidly increasing and in some centers approaches 60 years of age(1). Some parts of the United States reported that over 40% of all patients treated in 1982 were older than 60 years(2). Presently 20-25% of the patients are 70 years or older when started on dialysis(3). These patients have a high risk for atherosclerotic heart disease, peripheral vascular disease, chronic obstructive pulmonary disease, diabetes mellitus, malignant tumors and cerebrovascular accident (Table 1, Figure 1).

While the increased incidence of cancer (4,5), abnormality of lipid metabolism(6), abnormality of bone metabolism(7), and inhibition of immune system (8) in patients on maintenance hemodialysis have been reported, these problems may be related to the dialysis system itself in terms of biocompatibility and/or ineffectiveness of the therapy to remove so called "uremic middle molecules". The middle molecule" hypothesis is that these substances, thought to be uremic toxins and a cause of the above complications(9), may not be adequately removed satisfactorily by conventional dialysis method with the present cellulosic dialysis membranes(10).

Elderly patients, especially, are more susceptible to these complications and are likely to develop secondary disease conditions.

Therefore, the basic strategy for chronic dialysis in the elderly is to develop the most adequate and cost effective system, including several alternative treatments (Table 2). When compared to the hemodialysis cost in a dialysis center, home dialysis is much less expensive because it does not require the involvement of a doctor or a nurse. There is no reason to hesitate to start self-care dialysis even in the elderly patient(11). However, the number of patients who participate in home dialysis are appreciably lower than patients on center units(12). Miniaturization of the device can make it easier to perform home dialysis and also improve the social activity of the patient. Continuous ambulatory peritoneal dialysis (CAPD) is the one modality that has been shown to stimulate home and self-care dialysis.

In order to establish a more safe treatment modality, the development of membranes with improved biocompatibility is important. Improved dialysis sterilization methods, dialysate composition and anticoagulant type used for extracorporeal circulation also are important from the safety point of view. Utilization of new treatment modality will improve the effectiveness of detoxification, provide for a safer treatment and possibly reduce the overall cost of therapy.

It has been possible to treat diseases associated with the imbalance of small molecules as is done by hemodialysis for renal failure but it is now possible to treat various diseases associated with the imbalance of macromolecules. The recent introduction of membrane plasmapheresis makes selective removal of pathological macromolecules possible. On-line plasmapheresis technologies that have been developed include double filtration, cryofiltration(13), thermofiltration(14), and immunoabsorption(15). Utilizing these technologies, it is possible to treat autoimmune disease patients who have failed conventional drug therapies(16). Successful applications have included the treatment of rheumatoid arthritis(17). It is also documented that end-stage kidney disease and irreversible renal damage(18,19) can be prevented through various types of plasma treatment. Montoliu et al reported that three patients with mesangiocapillary glomerulonephritis treated by 4 liters of plasma exchange (10 to 16 times) showed improvements of renal function(18). Three patients with myeloma kidney who initially received treatment including furosemide, sodium bicarbonate and peritoneal dialysis with no beneficial effect were treated by 3 to 5 liters of plasma exchange 2 to 3 times(19). All the patients showed a marked improvement in renal function. The authors described that all therapeutic measures attempting to decrease serum light chain (Bence Jones) concentration may be of primary importance in management of acute renal failure in multiple myeloma. Since some of the chronic renal diseases that cause end-stage renal failures are of immunologic origin, it is assumed that they can be prevented through this technology. If this is possible, plasmapheresis treatment will not be an end stage treatment like hemodialysis which is required until the patient dies or is successfully transplanted. As described above, a limited number of plasmapheresis treatments can reverse kidney failure, and it may be possible to reduce the number of patients requiring dialysis treatments. By applying this new technology, it is hoped that the number of new dialysis patients can be substantially reduced. At this time, there are over 80,000 dialysis patients in the U.S. alone. The annual increase in the number of dialysis patients is over 5,000. If the plasmapheresis technology can reduce this figure by even one-half, certainly the total medical costs will be substantially reduced(20).

This same type of treatment may be applied for the prevention of atherosclerosis. At this time, the pathogenesis of artherosclerosis is not clearly understood. However, the relationship of hyperlipidemia and artherosclerosis is well documented. The treatment of hyperlipidemia is possible, using this new membrane technology. Thermofiltration, by its selective removal of low density lipoproteins, is now possible as demonstrated experimentally and clinically in patients in which drug or diet therapies could not control their lipid levels(21,22). As cardiovascular problems are among the most common in the elderly, the long-range impact of this treatment could be substantial.

The progression of end-stage atherosclerotic disease including coronary heart disease (angina and myocardial infarction), peripheral vascular disease, cerebrovascular accidents and atherosclerotic senile dementia could be suppressed or reversed. If this is possible, the progression of cardiovascular disease, which requires vascular prosthesis implantation or coronary bypass surgery, can be reduced.

Currently, one of the major candidates for the artificial heart is the victim of end stage artherosclerosis or cardiomyopathy. If the origin of the disease is such that plasma treatment can be utilized, certainly the number of potential candidates for the artificial heart can be reduced quite substantially.

Malignant tumor growth is believed to be related to a disturbance in the immune system and the build up of suppressor factors in the body. Publications have reported cases of plasmapheresis treatment for patients with malignant tumors(23). At this time, most reports are anecdotal. It is noteworthy that treatment periods were short, and there have been no long term treatment results reported. However, in combination with other traditional treatments such as immunologic, radiologic and drug therapies, the treatment of malignant tumors is more effective than without adjunct therapies. Reduction of mortality with this method of treatment has yet to be clearly documented.

In the past, the extracorporeal blood purification procedures were analogous to the artificial kidney treatment. However, the increased availability of more biocompatible and more porous membranes has expanded the capability of this method of treatment to a wide range of disease states. The availability of this technology makes possible more extensive studies increasing the chances of understanding and treating the pathophysiology of various diseases which are more likely to be associated with the elderly patient population. If this proves possible, the expense of treating the senile patient who is incapacitated, bedridden and not contributing to society can be reduced and the patient returned to a more enjoyable, productive life. The basic research, applied research and device development in this field is beneficial to our society.

II. PRESENT STATUS

2-A. Artificial Kidney

Artificial kidney has several modalities to treat renal failure patients (Table 3).

Hemodialysis is the extracorporeal detoxification system to remove excess body water, to correct abnormal electrolyte levels and to remove small to middle molecular size uremic substances. It does this primarily by diffusive solute flux (solute removal is based on the concentration gradient of the solute and the membranes permeability). The system is a combination of dialyzer (dialysis membrane), dialysate delivery system, blood pump, extracorporeal circuit and monitor. Dialysis is most effective in the removal of small molecular substances.

Hemofiltration is an extracorporeal blood system using a larger pore size, high flux membrane. Solute removal is by convective transport (bulk fluid removal). It requires dilution fluid rather than dialysate and is capable of removing more fluid and middle molecular uremic substances than in conventional dialysis.

Hemoperfusion is the extracorporeal detoxification system to remove toxic substances using absorbent. Blood is perfused over sorbents such as resins or activated charcoal.

Peritoneal dialysis is the system using the peritoneal membrane as a dialysis membrane by repeated infusion and drainage of dialysate to peritoneal cavity. The most commonly used scheme today is CAPD (continuous ambulatory peritoneal dialysis).

Also, combinations of different treatment modalities have been used to overcome the disadvantages of a single method. For example, hemodiafiltration (HDF) (convective and diffusive flux) can remove small and middle molecular substances with shorter treatment duration.

Miniaturization

Several methods have been developed to make dialysis systems more compact for the convenience of dialysis. Once uremia develops in citizens living in relative isolation, the options for life extension are reduced to self performed on-site regimens such as CAPD, home hemodialysis, or relocation of their home. Home dialysis can reduce the cost of hemodialysis and it is believed to be a better form of rehabilitation for the patient. Also, portable systems provide for more mobility of the patients and permit travel. Several portable systems have been developed. Junken Co. (Japan) and the University of Utah group developed the wearable artificial kidneys, WAK-III, which is composed of a pumping section and reservoir (18L). Over 200 clinical treatments have been performed out by dialysate recirculating system(24). The Univ. of Tokyo group has been working on the dialysate or hemofiltrate-regeneration system to develop really wearable artificial kidney using adsorbents with enzymes(25). Activated charcoal, ammonium adsorbent (reformed zeolite) and a urease column (for breakdown of urea to ammonium and carbon dioxide) are the main part of this device(26). Combined with pump sections, battery and reservoir, the total weight is 9 kg. The Univ. of Tokyo groups have also developed a urea adsorbent to reduce the weight of the WAK and simplify this system(27,28). A total system weighing 5 kg. is composed of a urea adsorbent, charcoal, ion-exchanger and pump sections. It is a promising system for WAK but is still in the pre-clinical stage.

Adsorbent

Innovation of an adsorbent system is important as a supplemental therapy for daily dialysis and especially for compact artificial kidney system. Urea treatment is the key for development of a wearable artificial kidney because of the difficulty of removing urea using small amounts of dialysate. Adsorbents are used both in the dialysate delivery system for regeneration of dialysate and in oral administration to patients as a supplemental therapy. The strategy of this therapy is to remove creatinine, uric acid and urea and the adjustment of electrolytes. Oral administration of newly developed oxystarch and activated charcoal is used effectively as a supplemental clinical therapy(29). It is known that oxystarch (dialdehyde starch: (DAS), having an activated aldehyde group on its surface can form a Schiff's base complex with urea or ammonium, and activated charcoal can absorb creatinine, uric acid and other non-polar middle molecules. To reduce urea, creatinine and uric acid effectively, 30 to 40 g of DAS and 25-50 g of activated charcoal are required to be administered per day, depending on patient requirements. When these adsorbents are used orally, surface coating is necessary to prevent damage of intestinal mucosa and decrease efficiency due to competitive adsorption of lipophilic substances in the bowel tract.

As a dialysate regeneration and a hemofiltrate regeneration the Redy system has been commercially available and used in clinical treatments(30) (Figure 2). The principle of this adsorption system is enzymatic decomposition of urea by urease and adsorption of ammonium by zirconium phosphate. Creatinine uric acid and middle molecules are removed by activated charcoal. The Univ. of Tokyo groups have modified this regeneration system using reformed Zeolite mentioned previously(26).

The major problems accompanied with dialysis in the elderly patient are poor blood access and an unstable cardiovascular condition due to extracorporeal circulation. Oral administration of adsorbents could be beneficial to the elderly because of no requirement of extracorporeal circulation and reduction of the frequency of hemodialysis. A miniaturization of the dialysis system with adsorbent allows for patient mobility during the procedures.

Continuous Ambulatory Peritoneal Dialysis (CAPD)

CAPD is a simple method using repeated infusion and drainage of dialysate using the peritoneal cavity (Figure 3). It utilizes the low dialysate flow rates and low volumes of dialysate. This allows portability, better creatinine dialysis than urea dialysis, and improved middle molecule clearances(31). This method is particularly useful for those patients who are capable of and interested in self dialysis(32). CAPD is reported to be as useful in the elderly as it is for the younger patient(11). This modality is particularly prone to a high rate of technical failure such as by infection, sclerosing peritonitis and access problems(32,33). Innovations to prevent these complications are being studied.

Membrane

Development of membranes of improved biocompatibility are needed (Table 4). Cellulosic membrane has a higher incidence of complement activation compared to synthetic polymer membranes(35). Activation of complement in the circulation results in pulmonary leukostasis and peripheral granulocytopenia(36). The impact of this effect is speculative but may be associated with the high infection propensity seen with end stage renal disease patients treated by hemodialysis(37).

Considering the middle molecule hypothesis, the attempt to develop a membrane for dialysis that would afford higher permeability of middle molecules (giving a theoretical justification of the shortened dialysis time) may be a logical and challenging choice(38).

Polyacrylonitrile (PAN) membrane dialyzers and fluid balancing equipment were developed between 1970 and 1972. The principal innovation of this membrane is its greater permeability to middle molecules and consequently, an ultrafiltration of approximately ten times higher than that of Cuprophan membrane. Between 1975 and 1976, polymethylmethacrylate (PMMA) membrane dialyzers were developed that are suitable for hemodiafiltration(39). Between 1977 and 1978, the cellulose acetate membrane gained a reputation for its excellent biocompatibility. Ethylenevinyl alcohol copolymer membrane (EVAL) was developed between 1978 and 1979. It showed a well balanced performance in removing low molecular weight and middle molecular weight substances and proved to be safer for the patient than the cellulosic membrane hemodialyzers. In general, these synthetics and modified cellulosics show improved biocompatibility (less reductions in blood cell counts, specifically, white blood cells and complement activation). Also, dialysis without anticoagulant infusion has been performed using synthetic EVAL membrane and improved blood lines(40). The latest innovation is the development of the polysulfone membrane between

1981 and 1982. This membrane has a high protein permeability and has lessened the complications attendant with chronic dialysis(41).

Despite the numerous studies done in this field, exact parameters defining overall biocompatibility in blood purification systems have not been well established. Global understanding for biocompatibility including whole system of complement, kinin-kalliklein, coagulation, and fibrolytic system must be considered(42).

Reuse and Sterilants

Dialyzer reuse has been proposed to reduce cost. However, evaluation of the savings obtained by reuse is not easy. Cellulosic membrane has been used with the innovation of automated systems for reprocessing hemodialyzers. It has been reported that with dialyzers reused up to 30 times clearance were unchanged(43). Also, hypersensitivity reactions so called "first use syndrome", occurs less often in re-use(44).

Ethylene oxide gas is recognized as one of the causes of hypersensitivity reactions(45). Steam autoclaving and x-ray sterilization is reported to have better biocompatibility(46). However, further examination in clinical study is required because high temperature and high energy may produce harmful degradation products.

Anticoagulant

Heparin is used as an anticoagulant even though it has an effect on complement activation(47), platelet function change(48), lipid metabolism(49), and bone metabolism. These biological effects are critical for chronic dialysis patients because of repeated usage. Recently, in place of heparin many new anticoagulant drugs have been used in hemodialysis. Prostaglandin I_2 is used to diminish platelet adhesion and aggregation(50). However, usage of PGI_2 is questionable in this stage due to its chemical instability and vasodilatory effect. PGI_2 analog (APS-306) is much more stable and has a lower vasodilatory effect than PGI_2. A highly selective synthetic thrombin inhibitor MD805(51), a new anticoagulant gabexate mesilate (FOY)(52) and a protease inhibitor 2-(6-Amidino) naphthyl 4-guanidino benzoate (FUT 175)(53) are being studied in order to control coagulability and platelet function except in those patients having bleeding diathesis. These new alternatives are to be used for the purpose of minimizing heparin dosage. Usage of these alternatives with biocompatible blood circuit and membranes may be feasible. Dialysis without anticoagulants has been tried(40).

Dialysate

multiple exposure to dialysate has problems in terms of biocompatibility during dialysis and chronic toxicity.

Dialysis using acetate as the dialysate buffer as opposed to a bicarbonate buffer(54) is reported to be associated with greater hemodynamic instability and various symptoms by means of metabolic changes and hypoxemia.

Quality control of dialysate for trace element is also important. Because the artificial kidney system cannot remove these trace elements combined with serum proteins, the toxicity due to these trace elements have to be removed by other means. Desferrioxamine (DFO), a chelating agent, is reported useful in the treatment of aluminum toxicity by mobilizing tissue aluminum stores in association with removal of diffusible aluminum in the dialysate(55). Also, the levels of magnesium and zinc in dialysate must be limited to prevent increases in their blood level(56,57). Dimethylnitrosamine, known as a precarcinogen, has been reported in dialysate water(58). This and other dialysate or water borne agents may have a relationship to the increased incidence of malignant tumors in dialysis population.

The innovation of a dialysate delivery system including a decrease in the volume of dialysate by adsorbent is thought to be an important step in minimizing problems associated with the dialysate.

Continuous Arteriovenous Hemofiltration (CAVH)

CAVH is the method to remove excess fluids in acute renal failure (Figure 4). High water permeable membranes are utilized for CAVH (Table 5). To prevent overloading of cardiac function, a hemofilter with small surface area and primary volume and minimum circuit length are required. Hemofiltration may be performed using the patient's own blood pressure without any blood pump with an exchange rate of about 100 ml/hr. This modality allows for hemodynamically stable withdrawal of excess fluid without the use of elaborate extracorporeal circuits(59). This method can provide nutritional supports essential for the treatment of multi-organ failure(60). It is especially good for elderly patients who are susceptible to developing multi-organ failure, and often present nutritional, metabolic, acid-base, electrolyte and hemodynamic abnormalities.

B. Plasmapheresis

The success of hemodialysis in the treatment of renal failure has promoted the development of extracorporeal technology for the therapy of other diseases. Diseases believed to be mediated by macromolecular weight substances such as circulating immune complexes, antibodies, low density lipoproteins, protein bound toxins, and others that accumulate in disease states have been treated by blood or plasma exchange since 1960.

Based upon early success in the treatment of various diseases by plasma exchange, its use in many diseases, and the use of the therapy for chronic treatment, the need for plasma products increases. Complications associated with their infusion, e.g. allergic reactions or infection, also increases. This stimulates the development of therapies that do not require plasma products. From the practical point of view, minimizing the need for plasma products can allow plasma treatments to be carried out more frequently, more extensively (processing larger volumes) and at lower costs. Because essential plasma components, as well as pathological ones, are removed during plasma exchange, techniques that are designed to remove only the pathological components are highly desirable. Techniques that have been investigated include sorption, physicochemical treatment, and filtration.

Sorbents

Sorbents have been developed and used in direct hemoperfusion for drug overdose, uremia, and liver insufficiency(61). Problems of biocompatibility and sorbent carry-over into the vascular system are overcome by means of on-line separation of plasma and plasma perfusion. Recently, several immunoabsorbents [Protein A(62), anti DNA antibody removal(63), heparin agarose LDL antibody(64), anti-A and anti-B antibody removal(65), polyvinyl alcohol gel(66), polymixin B fiber (endotoxin removal)(66), anti HBs antibody filter (Hepatitis B virus removal)(68)] have been developed for the treatment of immune disorders (Table 6).

Many kinds of charcoal and resin have been used for acute intoxication and liver failure including oral administration method(69).

Filtration

A simple treatment scheme, and one more universal in application, involves of the nonspecific removal of macromolecules in plasma. Membranes having a molecular cut-off of about 100,000 daltons allow the passage of albumin while retaining the macromolecular weight marker solutes. These schemes include cascade filtration, cryofiltration and thermofiltration (Figure 5).

Cryofiltration is the on line plasma cooling system to remove cryogel - a mixture of various types of macromolecules including fibrinogen, globulin fraction, immune complexes, antibodies and albumin(13). Clinical efficacy for rheumatoid arthritis and other autoimmune disease is reported(16,17).

Thermofiltration is the on-line filtration method kept near or above physiologic temperature to prevent cryogel formation(14). This treatment for hypercholesterolemia involves the selective removal of low density lipoproteins, so-called "atherogenic cholesterol", that is related to the incidence of coronary heart disease, while retaining albumin and high density lipoproteins; as called "antiatherogenic cholesterol" that has negative correlation to coronary heart disease(21). By means of modifying the abnormal lipid metabolism, this treatment modality may have impact on the progression and regression of artherosclerosis including coronary heart disease that is still the major cause of death and disability in the United States.

For cancer patients there are specific blocking factors or immunosuppressive substances for malignant tumors that exist in the patient's plasma(23). Also non specific blocking factors are reported. Aiming for reduction of these blocking factors, patients are treated by plasma exchange, but still results are controversial.

III. STRATEGY

The objective is to reduce the numbers of end stage organ failure patients through application of artificial organ technologies at much earlier stages in the disease process than has heretofore been possible. This will become more cost effective. The reduction in numbers of such patients will decrease the need for dialysis and transplantation. Reducing the incidence of end stage heart failure and occlusive arterial disease due to therosclerosis, vasculitis, or cardiomyopathy will lessen the need for artificial hearts and vascular or valve replacement. Preventing or slowing end stage bone and joint deterioration as related to long standing rheumatoid arthritis will decrease the need for artificial joints.

With the availability of artificial organ technologies, it is now possible to modulate the biochemical and immunological systems of the body. Chronic immunological diseases, including autoimmune diseases, atherosclerosis, cancer, and infection, can be treated by artificial organ technologies that regulate the body's bio-immunological chemicals, thereby halting and possibly reversing the disease process. While certain patients can be cured with or without the help of conventional medical or surgical therapy, in some groups of patients the number requiring treatment will certainly be reduced.

To reduce the cost of chronic dialysis, technological choices have to be made. Development of self-care systems including CAPD, more biocompatible materials (including membrane, dialysate, sterilant) and adsorbents and bioreactors (bacterial systems) as a supplemental therapy is thought to be an effective choice.

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LEGEND OF TABLES

1. Risk factor statistics (present at initiation of dialysis in all 157 patients(3).
2. Innovation in uremia treatment
3. Blood detoxification
4. Synthetic materials used for hemodializer and hemofilter
5. List of hemofilter for CAVH
6. Immunoadsorption systems described in the literature

TABLE 1

RISK FACTOR STATISTICS (PRESENT AT INITIATION OF DIALYSIS IN ALL 157 PATIENTS)[3]

Risk Factors Analyzed	Frequency	
Diabetes mellitis	17.2	
Arteriosclerotic heart disease (ASHD)	35.0	
Cerebrovascular accidents (CVA)	10.2	
Chronic obstructive pulmonary disease (COPD)	18.5	
Peripheral vascular disease (PVD)	22.2	
Nonskin malignancy (CA)	14.0	
In-center dialysis exposure time	79.9	
Home dialysis exposure time	17.2	100%
Satellite dialysis exposure time	2.9	
Program entry (patients entering prior to 1976)	19.7	
Sex (male)	52.5	

Mean entry year: 1978

Age: Mean 74.9 yrs Range: 70-87

TABLE 2

INNOVATION IN UREMIA TREATMENT

I. Apparatus	
1. Programable dialysis	
2. Multipurpose system	HD, HDF, HF
3. Miniaturization	portable, wearable, implantable
II. Dialyzer	
1. Shape	Hollow fiber
2. Sterilization	Autoclave, - radiation
III. Membrane	
1. Materials	Cellulosic synthetic
2. Structure	Thinner wall thickness
3. Biocompatibility	Less complement activation
IV. Dialysate	
1. Alkalin agent	Bicarbonate dialysis
2. Concentration	High sodium dialysis
3. Regeneration	(ex. REDY SYSTEM)
V. Anticoagulant	
1. New anticoagulants	FOY, FUT, prostaglandins
2. Non-anticoagulation	(ex. Kuraray's EVAL Dialyser)

TABLE 3

BLOOD DETOXIFICATION

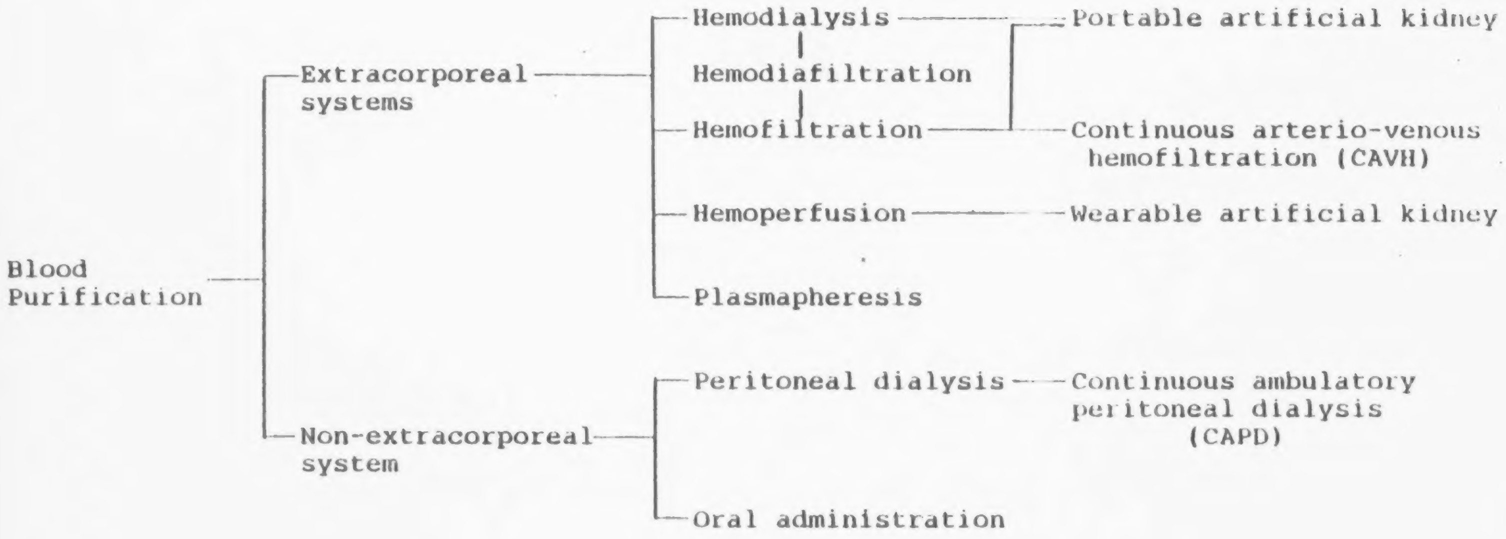
Blood Purification
Extracorporeal systems
Non-extracorporeal system
Hemodialysis
Hemodiafiltration
Hemofiltration
Hemoperfusion
Plasmapheresis
Peritoneal dialysis
Oral administration
Portable artificial kidney
Continuous arterio-venous hemofiltration (CAVH)
Wearable artificial kidney
Continuous ambulatory peritoneal dialysis (CAPD)

TABLE 4

SYNTHETIC MATERIALS USED FOR HEMODIALIZER AND HEMOFILTER

Material	Manufacturer
Polyacrylonitrile	Rhone-Poulanc (France)
Polymethylmethacrylate	Toray Ind. (Japan)
Ethylenvinyl alcohol	Kuraray Co. (Japan)
Polysulphon	Amicon Co. (USA)
Cellulose 2.5 acetate	Enku (FRG)

TABLE 5

LIST OF HEMOFILTER FOR CAVH

	Amicon	Asahi		Gambro		Toray	Renal	
	Diafilter-20	PAN50P	PAN60A	FH55	FH77	TK601	system	
Material	Polysulfone	PAN		Polyamide		PMMA	Polysulfone	
Module	HFAK	HFAK		HFAK		FHAK	HFAK	
Surface area (M^2)	0.25	0.5	0.6	0.6	1.4	0.3	0.25	0.5
Priming volume (ml)	20	42	50	43	90	26	25	50
Maximum TMP (mmHg)	500	500	500	600	600	500	500	500
Sterilization	EOG	EOG		EOG			EOG	

TABLE 6

IMMUNOADSORPTION SYSTEMS DESCRIBED IN THE LITERATURE

Immunoadsorbent	Substance Removed	Application	Author
Protein A	IgG IgG immune complexes	In Vitro	Rawer et al
Synthetic blood group B antigenic determinants	Anti-B antibodies	In Vitro	Chang
Glomerular basement membrane antigen	Anti-GBM antibodies	Dogs	Terman et al
Bovine serum albumin	Anti-BSA antibodies	Dogs	Terman
Protein A	IgG	Dogs	Terman et al
Heparin agarose	LDL	Dogs	Burgstaler et al
Anti-LDL antibodies	LDL	Pigs	Stoffel et al
Glutaraldehyde treated human erythrocytes	Complement components	Sheep	Schmer et al
Heparin agarose	LDL	Sheep	Schmer et al
Staphylococcus aureus Cowan I	IgG	Human	Bansal et al
DNA	Anti-DNA antibodies	Human	Terman et al
Staphylococcus aureus Cowan I	IgG	Human	Ray et al
Blood group A and B antigen	ABO antibodies	Human	Bensinger et al
Anti-LDL antibodies	LDL	Human	Borberg et al
Protein A	IgG	Human	Terman

LEGENDS OF FIGURES

1. Factors involved in the development of cerebral and cardiovascular disease in uremic patients and patients on dialysis.
2. Schematics of dialysate regeneration system (REDY).
3. Schematic of continuous ambulatory peritoneal dialysis.
4. Schematic of continous arteriovenous hemofiltration.
5. Schematic fo on-line plasma treatment.

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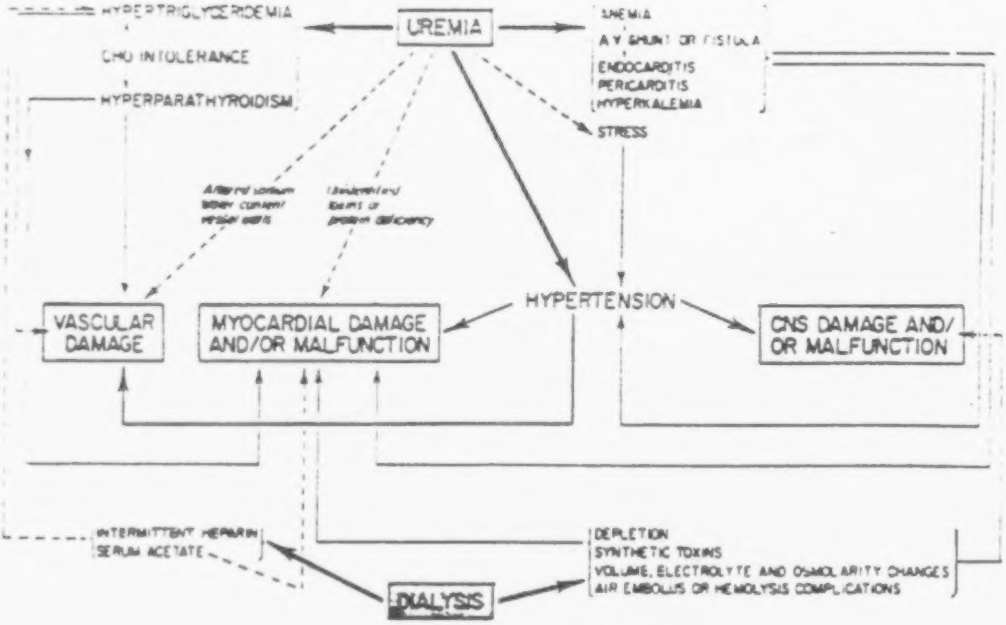
HYPERTRIGLYCERIDEMIA
CHO INTOLERANCE
HYPERPARATHYROIDISM
UREMIA
ANEMIA
A.V. SHUNT OR FISTULA
ENDOCARDITIS
PERICARDITIS
HYPERKALEMIA
STRESS
Altered sodium water content vessel walls
Unidentified toxins or protein deficiency
HYPERTENSION
VASCULAR DAMAGE
MYOCARDIAL DAMAGE AND/OR MALFUNCTION
CNS DAMAGE AND/ OR MALFUNCTION
INTERMITTENT HEPARIN
SERUM ACETATE
DIALYSIS
DEPLETION
SYNTHETIC TOXINS
VOLUME, ELECTROLYTE AND OSMOLARITY CHANGES
AIR EMBOLUS OR HEMOLYSIS COMPLICATIONS

Figure 1

Factors involved in the development of cerebral and cardiovascular disease in uremic patients and patients on dialysis.

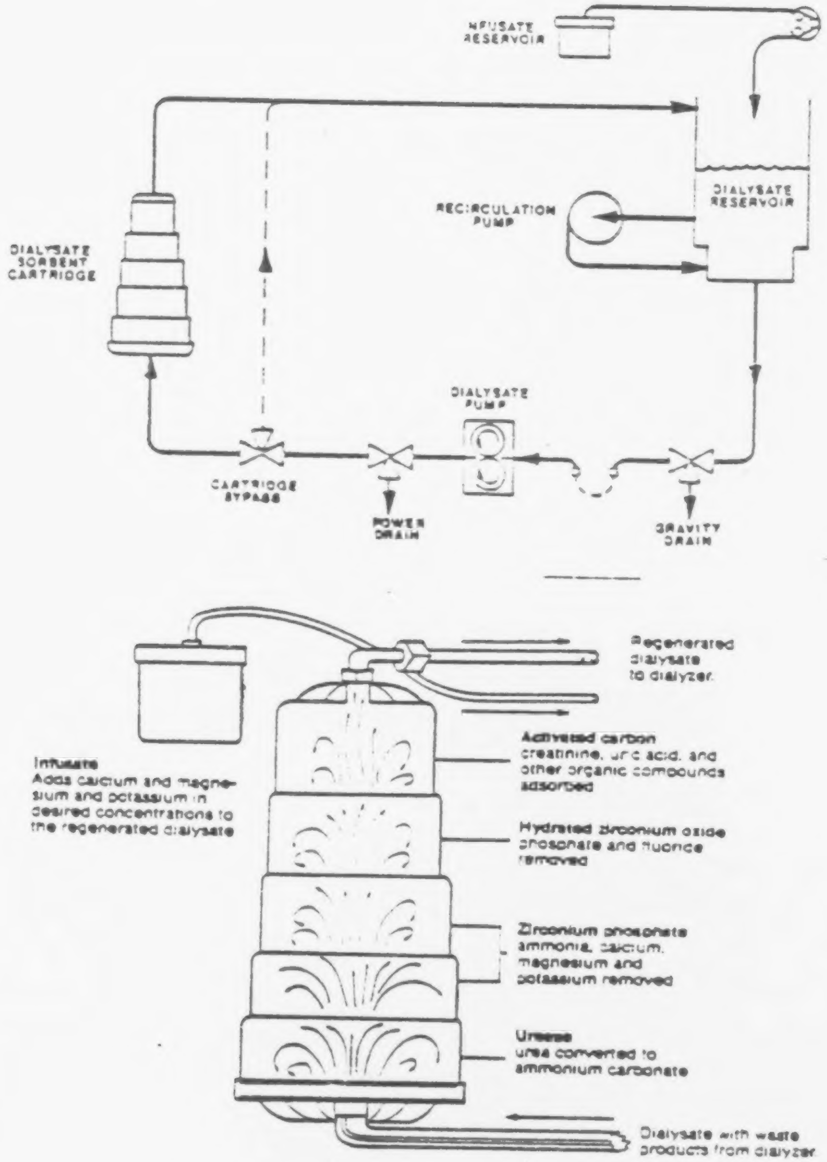
INFUSATE RESERVOIR
DIALYSATE RESERVOIR
RECIRCULATION PUMP
DIALYSATE SORBENT CARTRIDGE
DIALYSATE PUMP
CARTRIDGE BYPASS
POWER DRAIN
GRAVITY DRAIN
Regenerated dialysate to dialyzer.
Activated carbon
creatinine, uric acid, and other organic compounds adsorbed
Infusate
Adds calcium and magnesium and potassium in desired concentrations to the regenerated dialysate
Hydrated zirconium oxide
phosphate and fluoride removed
Zirconium phosphate
ammonia, calcium, magnesium and potassium removed
Urease
urea converted to ammonium carbonate
Dialysate with waste products from dialyzer.

Figure 2

Schematics of dialysate regeneration system (REDY)

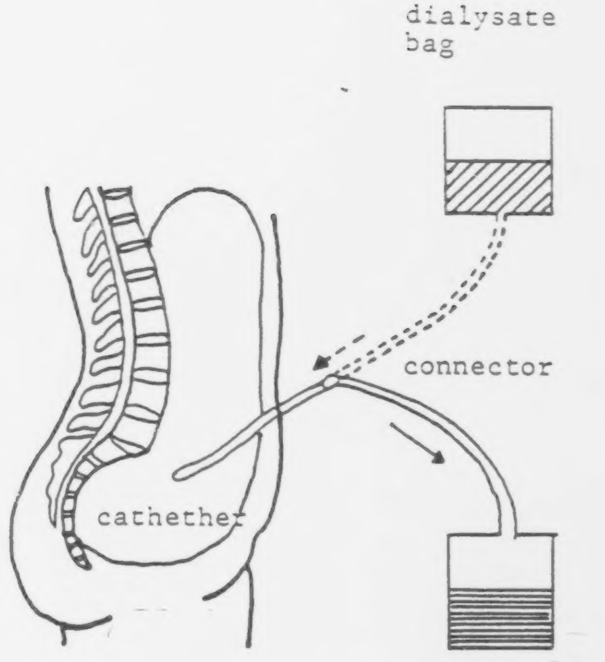

Figure 3

Schematic of continuous ambulatory peritoneal dialysis

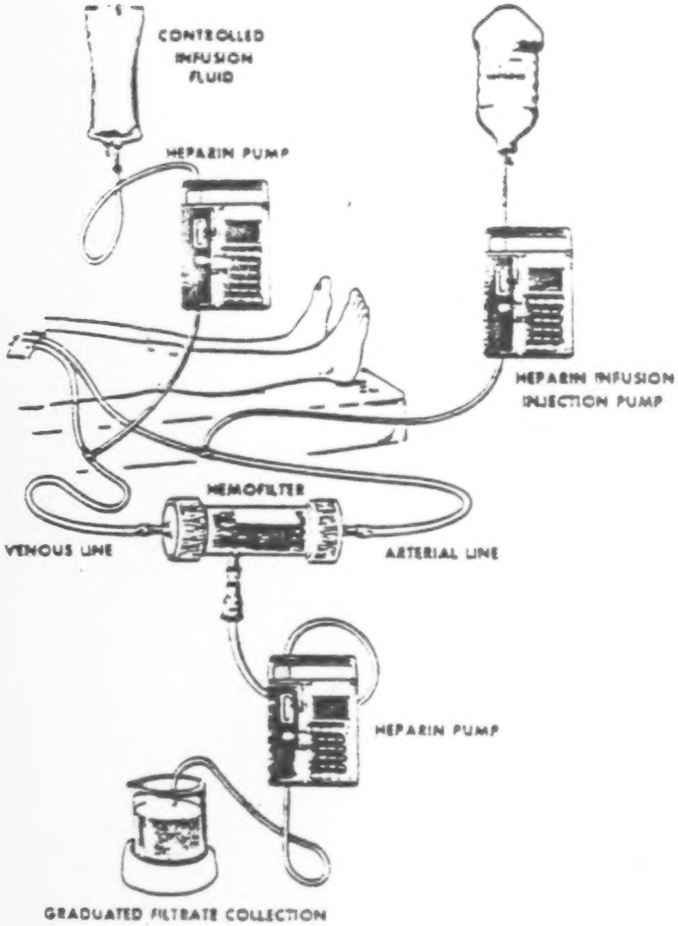

Figure 4

Schematic of continuous arteriovenous hemofiltration

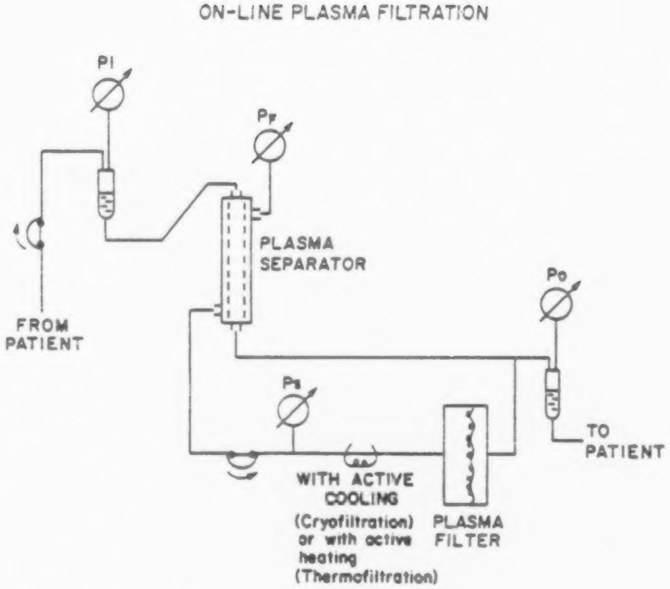
ON-LINE PLASMA FILTRATION
PI
PF
PLASMA SEPARATOR
FROM PATIENT
Po
Ps
TO PATIENT
WITH ACTIVE COOLING (Cryofiltration) or with active heating (Thermofiltration)
PLASMA FILTER

Figure 5

Schematic of on-line plasma treatment

TASK II: ADVANCES IN MECHANICAL VENTILATION TECHNIQUES

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I. Overview

The recent advancement in ventilatory technologies has introduced various types of reliable, effective simple to use respirators not only for hospital use but also for home use. Traditionally, the volume cycled ventilator is the main tool for this application. However, many other respiratory assist devices have recently been introduced. These include not only devices specifically developed for respiratory assist, but also other biomedical gas delivery devices that are available can also be utilized for this application.

Currently, portable pneumatic cardiac prosthesis actuators weighing less than 3 Kg are becoming available, and at least three such devices are available worldwide. One of the systems has been used successfully in five total artificial heart patients. It turns out that the gas delivery requirements for the portable pneumatic heart actuator and the portable respirator are similar, hence the requirement of lower pressures for the respirator enables developers to design a much more reliable and smaller portable respirator without the necessity of major technological innovations.

The recent introduction of jet ventilators, which can be made smaller and simpler, has the potential application for not only long-term ambulatory respiratory support, but also for left ventricular assistance if the ventilatory cycle is properly synchronized with ventricular diastole. A simple home use cardiopulmonary support system could be assembled in this fashion.

The recent advances ECMO (extracorporeal membrane blood oxygenation) technology imply that large portions of the respiratory failure patient population can be salvaged, as evidenced by the recent European group's studies. This technology enables the diseased lung to rest for a few weeks. Further development of the membrane oxygenator specially designed for ECMO purpose period much longer.

Recently, oxygenator technologies are switching from the traditional bubble device to the membrane oxygenator. The availability of more blood compatible gas permeable membranes guarantees longer and safer extracorporeal membrane oxygenation. Since the elderly population is more infection prone and more macromolecular abnormality oriented, improved blood compatibility of the system will be particularly beneficial in this group of patients. Another interesting technology introduced recently is total respiratory support using hemodialyzers rather than oxygenators. With several technical considerations, it is now possible to remove total adult body production of carbon dioxide from the blood employing a standard hemodialyzer. Consequently together with a hemodialyzer, total respiratory support can be established by only priming the alveoli with oxygen without respiratory movement.

Certainly these extracorporeal blood gas exchange systems will allow the respiratory systems to rest in order to heal some of the disease processes in the lung.

II. Available Mechanical Ventilation Technologies

Mechanical ventilation technologies have advanced such that chronic ventilatory support is a routine medical treatment. Both in the hospital and in the home the feasibility of assisted mechanical ventilation for the treatment of chronic respiratory insufficiency has been reported (1-8). The specific physiological benefits of long-term ventilatory assistance have also been documented (9-13). Patients with neuromuscular or musculoskeletal disease may often benefit substantially from such therapy and may thereby be permitted to live with a significantly improved quality of life, avoiding many of the prolonged hospital stays they might otherwise be required.

Several options are available to maintain adequate ventilation in the home. These include: a) volume-cycled ventilators; b) positive pressure breathing apparatus; c) oscillating beds; d) body respirators ("iron lung"); e) plastic wrap ventilation; f) chest-abdomen cuirass respirators; g) pneumobelts; and h) electrophrenic respiration.

a) The volume-cycled ventilator is particularly successful in patients with compromised respiratory mechanics. Sivak et al (1) recommended either the LP-4 ventilator (Life Products, Boulder, Colorado) or the PVV portable volume ventilator (Life Care Services, Boulder, Colorado) because of their portability (27 pounds each) and ease of operation. Currently, portable pneumatic cardiac prosthesis actuators weighing less than 3 kg are becoming available. One of these systems has been used successfully in five total artificial heart recipients. The gas delivery requirement for the portable pneumatic heart actuator and the portable respirator are similar, but the requirements of lower pressure for the respirator enables researchers to develop a much more reliable, smaller, portable respirator without any major technological innovations necessary.

b) The positive pressure breathing unit is an effective means of facilitating carbon dioxide elimination and preserving lung compliance. The pump is small and mobile and can be easily operated by a battery or house current and on room air by another person at home. It can be cycled automatically or by active inspiration. During waking hours it can be used intermittently or continuously, as needed. Humidified air is desirable if it is used more than 10 to 15 minutes at a time. In patients who require almost continuous mechanical ventilatory assistance during the waking day, a slower respiratory rate, a longer expiratory time interval in the respiratory cycle, and a positive pressure not exceeding 20 cm H_20 will minimize the undesirable reduced venous return to the heart associated with the application of positive pressure (3).

c) An oscillating bed provides ventilatory assistance by moving the diaphragm with gravity-induced abdominal visceral movements. Instead of reduced venous return to the heart, circulation is enhanced by the oscillation of the bed. The oscillating bed can ventilate the patient awake or asleep without any body encumberances. It provides a greater sense of personal freedom and is more physiologic. However, it may be most useful for patients with abnormal control of ventilation rather than compromised respiratory mechanics. Joos et al (14) reported improved ventilatory efficiency with the upper part of the rocking bed elevated 15° to 30°. Inkeley et al (15) pointed out that some diaphragmatic function is preserved in patients with late stage Duchenne dystrophy. Alexander et al (3) reported that effectiveness of the oscillating bed depended on the patient's ability to adapt his rate of ventilation to the oscillations of the bed.

d) Prolonged intermittent use of body respirators, such as the "iron lung", is beneficial for patients with progressively severe hypercapnia secondary to obstructive lung disease, Kyphoscoliosis or poliomyelitis (5,6). In contrast, intermittent positive pressure breathing (IPPB) has little effect on chronic respiratory failure in obstructive lung disease (2,3,4). Rochester et al (13) pointed out that body respirators diminish inspiratory muscle electrical activity and indicated that these respirators assume the work of breathing and provide a rest for the overburdened inspiratory muscles. The immediate benefit is a relief of dyspnea. It is also possible that the reduction of inspiratory muscle energy expenditure which results from body respiratory therapy improves the function of these muscles and thus contributes to clinical improvement in patients with chronic progressive respiratory failure (3).

e) Plastic wrap ventilation is similar to ventilation with body respirators or the "iron lung". The patient, lying in bed, is placed in a polyurethane wrap which completely envelopes the body except for the head. A pump connected to the wrap intermittently creates negative pressure inside the wrap. An arched, metal screen support rests on the bed, inside the wrap and over the thorax and prevents the plastic from lying directly on the patient's chest and allows freedom of respiratory expansion. Like the oscillating bed, the plastic wrap respirator affords continuous ventilatory support and limits mobility. Patients find it functional and comfortable for sleeping and resting (3).

f) The chest-abdomen cuirass works on the same principle as the plastic wrap ventilator. It creates a negative ambient (extrathoracic) pressure and acts as a bellows mechanism. The unit allows mobility, as it can be operated from a wheelchair-mounted battery or from an electrically-powered wheelchair (3).

g) The pneumobelt (intermittent abdominal pressure respirator) is another means of providing mechanical ventilatory aid. It produces increased external abdominal pressure which cause active expiration and augments passive inspiration. An elastic expandable, flat bladder incorporated within an abdominal corset is inflated with 50 cm H_2O positive pressure. The corset compresses the abdominal wall and causes the diaphragm to rise and forced exhalation to occur. Inspiration follows with deflation of the bladder and descent of the abdominal viscera. To be maximally effective, the patient must be in a sitting position of at least 75° (16). The unit also allows a good deal of mobility, as it, like the chest abdomen cuirass, can be operated from a separate battery carried on a wheelchair or from the battery of an electrically-powered wheelchair (3).

h) Electrophrenic respiration is an effective form of long-term management in primary alveolar hypoventilation (11, 17-21). Glenn et al (18,22,23) have reported their experiences with electrophrenic respiration, with a total of 53 patients, thirty-seven of whom were quadriplegic. The longest duration of continuous support by electrophrenic respiration was 5 years. Hyland et al (11) reported that one phrenic nerve stimulation allowed to maintain adequate ventilation with normal ventilation-perfusion rate. Electrophrenic respiration can provide effective long-term treatment of alveolar hypoventilation of both the central and primary types with proper selection of patients and careful placement of the phrenic electrode.

The application of mechanical ventilation in the home care setting can be traced as an evolutionary process. It should be emphasized that not all patients are suited for long term support (8,24). Although Sivak, et al have demonstrated that home care is less expensive (25), some consideration must be given to the long term goals of home care. The clinical course of respiratory deterioration usually dictates either that mechanical ventilation will be rehabilitative, (that is, provide the hope of rehabilitation and a returning to a previous life style) or that it will be only supportive and preserve intellectual function and physiological well being (1,26). As emphasized by Sivak, careful preparation for home care (27) and proper patient classification (28) is necessary for proper technological application of mechanical ventilation in the home.

III. New Types of Mechanical Ventilatory Assist Technologies

In spite of the striking efficacy and safety of mechanical ventilation, the method involves considerable deviation from the normal physiological mechanism of respiration (29). When used improperly or on patients incapable of compensating for the almost inevitable though usually minor disturbances which result from interference with normal bodily processes, mechanical ventilation may become harmful to a significant degree, resulting in: a) harmful cardiovascular effects (30-43), b) damage to the lungs (44-48), c) uneven ventilation (49-50), d) disturbances of acid-base balance, e) cerebral vasoconstriction (51-59) and f) renal, hepatic effects (60). Minimizing these harmful effects is absolutely necessary in order to advance the state of the art in mechanical ventilation.

Inspired gas reaches the alveoli by a combination of convection and diffusion. Gas transport is classically approached in terms of cyclic ventilation where most of the transport of fresh gas is achieved by bulk flow through the airways, with mixing throughout the large alveolar compartment by diffusion (61). Conventional ventilators have tended to mimic this pattern of respiration by using normal breathing frequencies and applying either positive pressure at the airway or negative pressure around the thorax to induce the convective transport of fresh gas into the lungs (61). The conventional management of patients in respiratory failure is to enhance convective flow. However a conventional ventilator does nothing to enhance diffusion (62). Furthermore, application of high pressure to a lung with nonuniform distribution of time constants may damage the lung, especially in elderly patients who have chronic obstructive lung disease. For example, pneumothorax, pneumomediastinum or subcutaneous emphysema may occur in the elderly patients' lung.

Recently, high-frequency ventilation (HFV) has appeared based on the concept that oscillatory flow can accelerate diffusion and is adequate for gas transport (62). HFV is a form of mechanical ventilatory support that differs from conventional modes of ventilation in both its relative tidal volume (Vt) and respiratory rate (63). HFV uses tidal volumes less than anatomic dead space at frequencies considerably greater than normal (up to 40 Hz).

A number of investigators have offered definitions of HFV based on respiratory rates.

1) high-frequency positive-pressure ventilation:
respiratory rate = 60 - 110 breath/min

2) high-frequency jet ventilation:
respiratory rate = 110 - 400 breath/min:

3) high-frequency oscillation:
respiratory rate = 400 - 240 breath/min

This HFV has relevance for elderly patients based on the following experimental and clinical results.

1) During conventional mechanical ventilation, the distribution of ventilation is governed mainly by the regional lung compliances. However during HFV, the lung compliances become relatively unimportant (63). Elderly patients usually have problems in lung compliances.

2) For the same mean airway pressure, the degree of barotrauma in the lung might be less during HFV than conventional mechanical ventilation because of a decrease in both peak pressure and phasic lung distension (64).

3) In several patients there was an improvement in gas exchange during HFV as compared with their standard form of mechanical ventilation (62).

4) Large tidal volumes by conventional mechanical ventilation deplete the surfactant in the lung faster than small tidal volumes by HFV (65). HFV may augment lung stability at least in diseased elderly patient's lungs by preventing atelectasis and minimizing changes in tissue and surface forces.

There are three kinds of systems used in HFV delivery 1) open system 2) closed system 3) pleural surface system (63).

1) Open System

Open ventilator systems are those in which there is a port left open to the atmosphere at all times to allow the escape of respired gases. The advantage of this system is that they require no pneumatic seal at the airway opening. However the disadvantage of this system is that the gas pressures and flows achieved in the airway may be dramatically altered by interventions that alter pulmonary impedance (63). Currently there are three major types of open-system devices: a) jet ventilators, b) flow interrupters c) oscillators. In both a) and b), gas from a high-pressure source is allowed to flow into the airway for a given length of time. Oscillator-type ventilators consist of a piston driven by a motor, which creates a to and fro movement of gas within the airway.

2) Closed Systems

The airway in the closed system differs from that in the open system in that it is isolated from atmosphere during the inspiratory phase of the ventilator cycle, thus assuring that the total tidal volume generated by the ventilator enters the respiratory system (63). There are two major types of these closed systems: a) valved ventilation and b) oscillator type ventilation. Solenoids or rotating valves are used in valved ventilation. Electric motors or high air pressure source are used in oscillator type ventilators. Recently, Ngeow and Mitzner (66) have developed a new type of closed oscillator type ventilator that is completely sealed and thus has the advantage that oscillatory volume cannot leak from the system. A portable HFV system has been developed at NU-TECH Industries, Inc. using miniature brushless DC motors under a NIH grant. A improved respirator system with a portable configuration, high reliability and simple control features could treat patients at home on a long term and unsupervised basis without the sacrifice of their mobility. The unit will provide the chronic obstructive pulmonary diseased elderly patients with 5 to 10 L min of extra ventilation without increasing the work of breathing on the part of the patient.

3) Pleural Surface System

This system employs oscillations that are used at the chest wall rather than at the airway. This has the advantage of not requiring airway access but the disadvantage that the transfer of oscillatory energy to the lung may be technically difficult. This technique may ultimately prove to be valuable in applying ventilatory assistance in elderly patients with incipient respiratory failure.

IV. ECMO (Extracorporeal Membrane Lung Oxygenation)

Life threatening pulmonary failure not responsive to conservative therapy is routinely treated with mechanical ventilation. However this method has its limitations.

ECMO is a treatment for pulmonary failure considered irreversible by current medical treatment using an extracorporeal membrane lung oxygenator. Oxygenation to, and CO_2 removal from the blood are achieved via passive diffusion in a membrane similar to that used in hemodialysis. By preventing hypoxia and hypercapnea, the membrane lung can maintain life while otherwise intolerable pulmonary damage heals. Repair may be possible because appropriate levels of extracorporeal support can relieve the patients lung of their primary burden of respiratory gas exchange and of the handicaps of conventional therapy: high airway pressures and high oxygen concentrations.

ECMO enables elderly patients to create a better environment in which the diseased lung can recover. The lungs are now free to be treated directly with bronchoscopy, pulmonary lobe irrigation and locally applied antibiotics, steroids or detergents, rather than just waiting for the diseased lung to recover. Many kinds of membrane are used experimentally aiming for improved ECMO system. These are shown in Table I.

Historically Willem Kolff first described blood oxygenating across the cellophane membrane of his artificial kidney (67) in 1944. Since then, the development of the gas exchange device has undergone a rapid evolution in search of an efficient, safe, simple to use and economical device that would accomplish the needs of extracorporeal oxygenation during open heart surgery. In 1983, 75% of the marketplace used bubble oxygenators, 25% used membranes. A dramatic shift has occurred in the last two years. Currently, 56% of the market place uses bubble oxygenators, while 44% use membrane oxygenators. Today, we are in the age of the membrane oxygenator. Currently, there are ten membrane oxygenators available in the market and there are only four bubble oxygenators still in commercial use (Table II).

In 1956, Dr. Kolff and Effler (68) developed a coil type membrane oxygenator, using the technology Kolff described in the cellophane membrane of his artificial kidney. This ciol type membrane is a predecessor of the Sci-Med or coil membrane (69), although modified, but still clinically available today.

In 1969, Lande made a commercially available plate type membrane. The plate technology is still used in membranes today.

This plate technology continued through the mid 1970's on the Travenol membrane oxygenator when it became a clinical reality. The Travenol membrane and the Kolobow Sci-Med membrane are the last survivors so called the "first generations of membranes".

As we entered a "second generation" of the membrane oxygenator, two types are currently available namely the hollow fiber and flat sheet type (71).

As early as 1968 there is a design described from a parallel bundle of capillaries were surrounded by a central oxygenating mannifold. Gas circled among these fibers as blood went through the fibers. However, the high cost, blood flow limitations, poor CO_2 transfer and large surface area has precluded the clinical use of such a device. It was not until Suma and Associates (72,73) in Japan reported a newly developed polypropylene hollow fiber oxygenator (Figure 1) made by Terumo in 1981 (74). Another example of a hollow fiber device is the one with an external blood flow. What that means is that the blood flow around the fibers and gas flows through the fibers. This is a Maxima hollow fiber oxygenator made by Extracorporeal. The fiber bundle is composed of polypropylene hollow fiber wound around a core, encases in a polycarbonate shell. The effective membrane surface area is approximately $2m^2$. The advantage of such a device is that it has a reduced priming volume of 480 ml and basically one size fits all patients. This device was used for patients with recommended flow rates of 1-7 liters per minute.

The Bard membrane is another example of an external blood flow hollow fiber. This device has integrated heat exchanger, a coiled type, as well as a built-in collapsible venous reservoir, which is a closed system.

The flat plate technology is made up of either porous or non-porous material. The Sci-Med oxygenator is of a non-porous, coil type membrane. The true example of a flat plate membrane is the Travenol membrane lung or TMO, as mentioned earlier. The TMO became a reality in the mid 1970's and there are some institutions still using the device today. However, it does not seem that simple to use. Travenol, realizing that the TMO's limitations, complexness, because of its external heat exchanger, two pump system, developed the LPM-50. The Low Pressure Membrane 50 uses the parallel plate configuration of its father, the TMO. Another example of a flat plate membrane is the Cobe membrane lung, CML. The Cobe membrane oxygenator has a 2.25m^2 surface area of polypropylene. This oxygenator has an integral, coil type heat exchanger.

The Interpulse membrane oxygenator by Extracorporeal requires a large piece of permanent equipment called "the pulser". The Interpulse is equipped with a pulsing device that augments secondary flow in the blood path and thus enables the manufacturer to utilize only 0.8m^2 surface area of a teflon-like material as a membrane. The pulsing effect of the oxygenator is used to expose the blood elements to the minimal oxygenating surface. The Extracorporeal "shake and bake", as it was called, was short lived in the clinical arena. Much of the attention of Extracorporeal came to develop their hollow fiber Maxima, which was described previously. The Shiley oxygenator is a rectangular shaped membrane, with an integral heat exchanger. It has a surface area of approximately 2.3m^2. The sheet is folded in about 60 blood flow and 61 gas flow channels, separated by a non-woven screen spacer. As blood enters the flow channels, it encounters innerdigitalization of the blood and the gas screen spacers. This creates a passive secondary flow pattern and causes an intermixing of the blood layers and greater exposure of the blood elements to the surface of the membrane. This is the last participant of the flat plate membranes.

All of these membrane oxygenators have been designed and developed mainly for the short-term usage during open heart surgery. As compared to the bubble oxygenators, the membrane lungs have been shown to elicit less trauma to the blood elements and thus made extracorporeal circulation safe for more than several hours. However, the interaction of blood with an artificial sruface used in a membrane oxygenator inevitably causes various adverse effects including complement activation with subsequent platelets and leukocytes sequestration in major internal organs. Biological substances released from these cells are believed to constrict and/or obstruct the regional blood vessels, change their permeability, and cause damages in tissues including the lung. Most of all, extracorporeal circulation with oxygenators requires heavy systemic anticoagulation of patients, which is responsible for bleeding complication in approximately 50% of patients receiving ECMO. The patient is required to be hospitalized, and the procedure is carried on for maximum of weeks in the intensive care unit requiring extensive monitoring and continuous supervision. Therefore, this technique is currently applied only to a patient group with reversible acute respiratory failure, and has little therapeutic value for home-stay patients with chronic progressively deteriorating respiratory insufficiency. In light of a steady increase in death rate due to the progressive obstructive pulmonary disease among the elderly in the United States, a development of an ECMO system aimed for this latter group of patients appears to be mandatory.

In spite of the striking efficacy of ECMO in oxygenation and CO_2 removal, veno-arterial ECMO associated with continuous positive pressure ventilation has failed to improve survival in severe acute respiratory failure patients (75). There were two factors in this ECMO failure; 1) the use of veno-arterial bypass with proportional decreases in pulmonary perfusion, 2) the use of high pressure continuous positive pressure ventilation resulting in focal pulmonary alkalosis and barotrauma in the underperfused diseased lung (76).

Gattinoni et al (76-78) has applied a new approach to the treatment of acute respiratory failure by dissociating the two main respiratory functions, i.e. CO_2 removal and oxygen transport. CO_2 extraction was assured by use of an extracorporeal membrane lung through a low flow veno-venous bypass, thus preserving pulmonary blood flow. Oxygen transport was provided by diffusion through the diseased natural lungs ventilated 2 to 3 times/min to preserve pulmonary mechanics and volumes (Low Frequency Positive Pressure Ventilation with

Extracorporeal CO_2 removal, LFPPV-$ECCO_2R$, Figure 2). The goal of this technique is to prevent ventilation-perfusion mismatching in nonhomogeneous lungs through lung static inflation and to avoid the local and systemic complication of continuous positive pressure ventilation, while providing a better environment for lung healing.

The combination of high frequency ventilation (HFV) and ECMO enable us to establish a new concept; one in which CO_2 removal and oxygen transport will be achieved by HFV, and additional oxygenation and CO_2 removal are accomplished by a low flow veno-venous gas exchange system. It has been also recognized that oxygenation of blood occurs somewhat during hemodialysis, but hemodialyzers are quite effective for the removal of CO_2. With the blood flow of 400 cc/min, it is possible to remove as much as 50% of CO_2 production. Using a hemodialysis membrane for this method enables us to perform the serial exchange of O_2/CO_2 and solutes/water respectively in elderly patients. Management of elderly patients will be simplified by this technique, and cost-performance will be enhanced. In order to avoid lung edema, continuous arterio-venous slow ultrafiltration is proven to be effective. Small effective ultrafilters are currently available. Currently, an ideal oxygenator for ECMO purpose is not available. They are functionable but it is only less than 30 hours. In order to develop an oxygenatior for this application following criteria should be applied.

1. Gas exchange capability lasting more than 1 week and easily replaceable.

2. Small surface area with more biocompatible membrane.
3. Development of simple, small atraumatic pump applicable for one month.
4. Simple and small priming volume system.

Ideally this system can be operated with minimum or no anticoagulating agent. The development of a portable,simple to use ECMO system, which requires no or little anticoagulation, would make it possible to treat many patients with chronic progressive respiratory failure at home. Synonymous to this would be the prevalence of home dialysis. Currently 14 to 18% of patients with end stage renal disease are treated with this remedy with less cost and more acceptable quality of life.

V. Peritoneal oxygenation and CO_2 removal

Theoretically, peritoneal gas exchange of O_2/CO_2 is possible like that in peritoneal dialysis. Although oxygen transport characteristics of the peritoneal membrane is known to be small, augmentation can be expected by utilizing artificial blood with high oxygen carrying capacity. Artificial blood is saturated with oxygen and pumped into the peritoneal cavity. Oxygen then diffuses down a concentration gradient into the tissues and blood supply of the peritoneum (79). Recently a hemoglobin conjugate has been developed as an oxygen carrying blood substitute at Ajinomoto CO, Japan (80). Now in-vivo studies of this artificial blood are being performed with excellent results at the Department of Artificial Organs, Cleveland Clinic. This artificial blood may be applicable for peritoneal oxygenation.

On the other hand, it is well known that substantial carbon dioxide can be removed during a standard hemodialysis as described previously. In a recent study it is also suggested that hypercapnia can be corrected by closed loop, re-circulation peritoneal dialysis with chemical extraction of CO_2. This simple paracoporeal technique is able to remove at least 33-50% of resting human CO_2-production (81). For respiratory assistance purposes, artificial blood can be utilized instead of conventional dialysate. The artificial blood has certainly a higher CO_2 affinity than dialysate, and oxygen supply to the peritoneal cavity is accomplished simultaneously. This peritoneal oxygenation and CO_2 removal could enhance the weaning of elderly patients from mechanical ventilators and could be used in non-hospital settings similar to that of peritoneal dialysis. These methods can enhance the quality of an elderly patients' life because they could be free from trachial intubation.

VI. Implantable Artificial Lung

There are three broad classes of membrane lungs, based on the resistance they offer to blood flow: the first is high flow resistance (more than 200 mmHg at 4 L/min blood flow rate) and is used only with a pump on bypass; the second is moderate flow resistance (up to 100 mmHg at 5 L/min blood flow rate) and is used with a pump on V-A bypass, or can be used with or without a pump on A-V bypass; and the third is low flow resistance (less than 20 mmHg at 2 L/min blood flow) which could be considered for use as a booster lung as a unilateral implant in parallel with the natural lung, with the blood flow driven by the pressure generated by the right ventricle.

Six aspects of design for implantable lungs should be considered (82). The first aspect is the provision for adequate gas transport. The second is avoidance of thrombus formation. The third is the prevention of tissue disposition or overgrowth on the membrane. The fourth provision concerns ventilation. This need not be made via a connection to the bronchi or trachea but could be done via a stoma in the chest wall. The fifth is drainage of fluids from the gas space. An implanted artificial lung would not have cilia to move material towards the trachea, nor would it have the ready capability for absorbing fluids. However, a drainage system could be incorporated fairly easily. The sixth is removal of airway particulates by facilitating lavage (82).

Recently the extracapillary flow type hollow fiber membrane oxygenator in which blood flows outside and gas passes inside of hollow fibers has been developed. Since this type of hollow fiber has low flow resistance, pumpless ECMO for total right ventricle to left atrium bypass could be done (83). At this stage, no existing membrane lung is suitable for this purpose. Collaboration among many disciplines is required for the development of an implantable artificial lung. Blood compatible biomaterials, which necessitates no or little anti-coagulation under a low blood velocity, is to be developed. The materials should be strong enough without rupture when made in a very thin structure, should be moldable to yield fine cappillary structures, and above all, should be quite permeable to oxygen and carbon dioxide but not to water. This artificial lung would require an implantable ventilator, which facilitates gas movement in and out from the device, since respiratory muscles may not be usable for this purpose.

The heart and lung frequently fail simultaneously due to the extensive interaction of these closely related organs. It seems reasonable to consider the design of a combined artificial heart and lung prosthesis (85). We are at the stage where we can envisage reasonably that an implantable total artificial heart could be available in the early 1990's. The NIH has just recently issued Request for Proposal to develop completely implantable total replacement and biventricular bypass systems. Accomplishment of this program will certainly facilitate the development of an implantable artificial heart and lung system.

Recent progress in organ transplantation technology has enable to bring lung transplantation into clinical reality. Although short term clinical results appear to be promising, only few facilities in the the United States are currently performing this procedure. Similarly to cardiac transplantation, absolute lack in donor population is the major drawback in this modality, together with problems in rejection and infection. Increase in aged population is a common feature in every developed country in the western world. Death rate from chronic lung disease has been steadily increasing. Unfortunately pathology of the lung in the most of this population appears not to be reversible. There is an urgent need to develop a total replacement device of lung function, which is preferably implantable. The criteria for an artificial implantable heart and lung are: 1) capability of physiologically adequate blood pumping and gas exchange, 2) provision for maintaining membrane surfaces free of deposits; and 3) damage to blood components should not exceed the capacity of the body to dispose of and renew them.

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LEGEND OF TABLES

Table I	Currently available membranes for ECMO.
Table II	Membrane and bubble oxygenators currently in commercial use.

TABLE I

1. Dense membrane
    - a) Silicon rubber
        - i) Polydimethylsiloxane
        - ii) Dimethylsiloxane-carbon block copolymer
        - iii) Polyfluorosiloxane
        - IV) Polydiphenylsiloxane
    - b) Polyalkylsulfone
2. Microporous membrane
    - a) Polytetrafluoroethylene
    - b) Polypropylene
    - c) Polysulfone
3. Combined membrane

   Polypropylene + silicone/polyalkylsulfone

TABLE II

OXYGENATOR	MANUFACTURER	PRICE ($)	MEMBRANE MATERIAL	CONFIGURATION
TRAVENOL TMO	BAXTER/TRAVENOL	405	POLYPROPYLENE	FLAT-PLATE, ACCORDIAN PLEATED *
TRAVENOL LPM-50	BAXTER/TRAVENOL	434	POLYPROPYLENE	FLAT-PLATE, ACCORDIAN PLEATED *
SARNS/OMNIS HF	OMNIS (SARNS)	N.A.	POLYPROPYLENE	HOLLOW-FIBER (EXTERNAL BLOOD PATH)*
CAPIOX II	TERUMO	419	" "	HOLLOW-FIBER (INTERNAL BLOOD PATH)*
INTERPULSE	J&J	395	" "	FLAT-PLATE, PARALLEL SHEET, SEPARATE*
MAXIMA	J&J	395	" "	HOLLOW-FIBER (EXTERNAL BLOOD PATH)*
H-4000	BARD	425	" "	HOLLOW-FIBER (EXTERNAL BLOOD PATH)*
BOS-CM	BENTLEY	464	" "	HOLLOW-FIBER (INTERNAL BLOOD PATH)*
M-2000	SHILEY	415	" "	FLAT-PLATE, ACCORDIAN PLEATED *
CML	COBE	410	" "	FLAT-PLATE, ACCORDIAN PLEATED *
SCI-MED I	SCI-MED	435	SILICONE RUBBER	SPIRAL-COILED, CONTINUOUS SHEET **
SCI-MED II	SCI-MED	N.A.	" "	SPIRAL-COILED, CONTINUOUS SHEET **

* MICROPOROUS
** NON-MICROPOROUS

LEGEND OF FIGURES

Figure 1 Hollow-fiber membrane oxygenator. Gas exchange area, 5.4m^2 peociws vy 60 x 10^3 fibers of polypropylene.

Figure 2 LEPPV-ECCO$_2$R Technique (from Pesenti A, et al. Trans Am Soc Artif Intern Organs 1980;26:550).

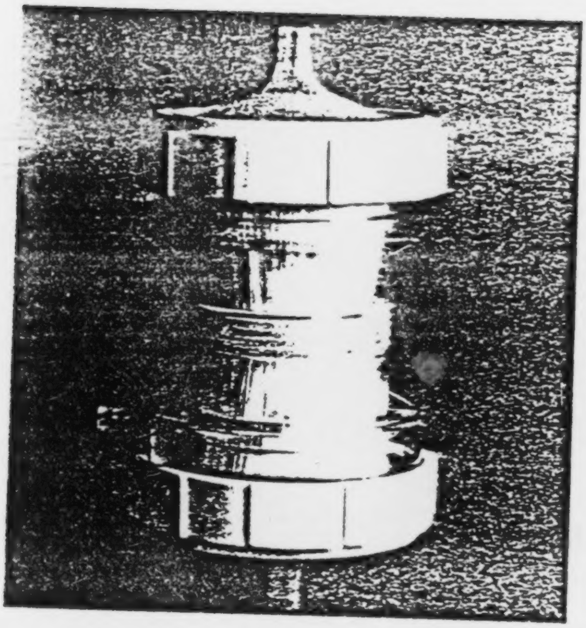
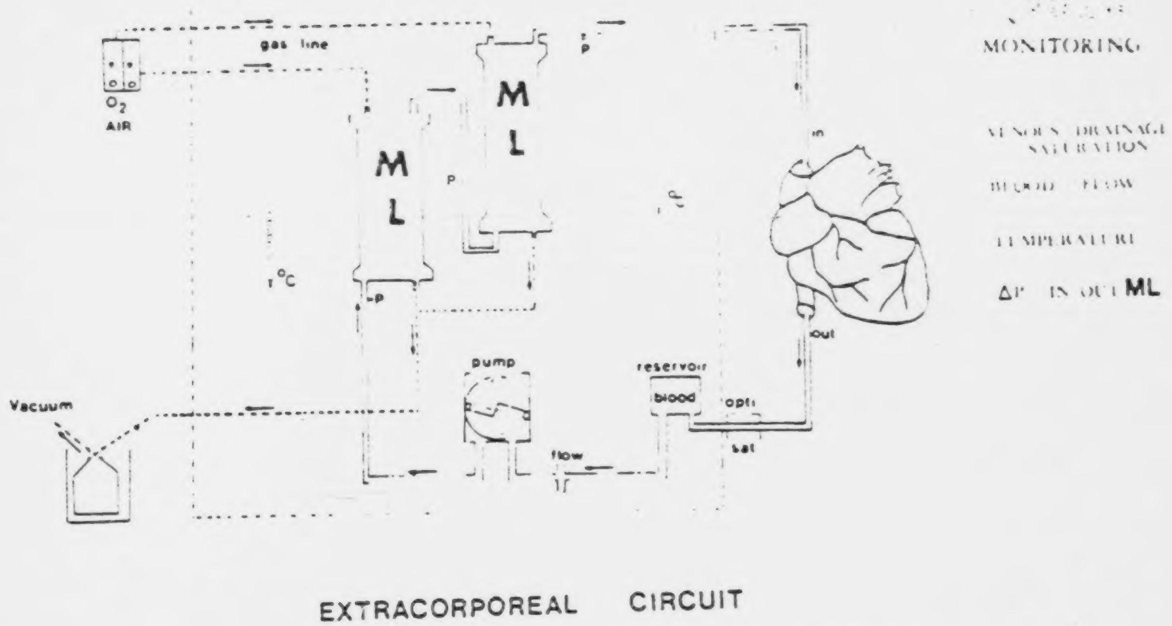
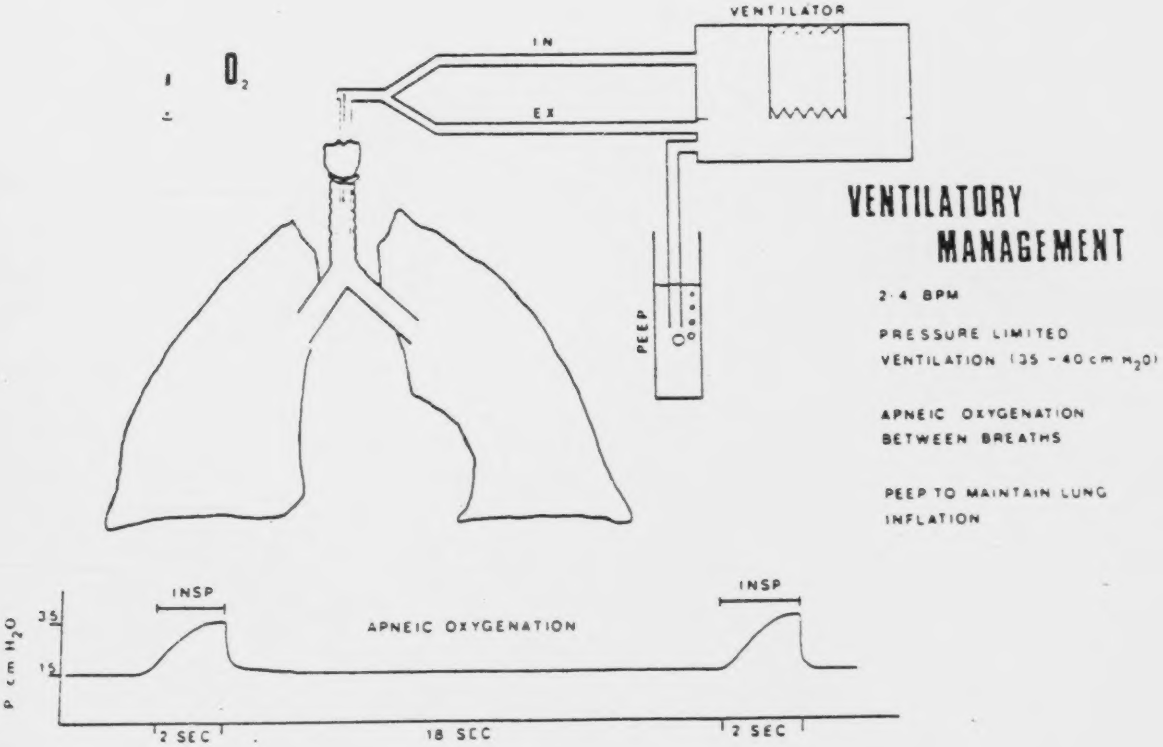


Figure 1 Hollow-fiber membrane oxygenator. Gas exchange area, 5.4m^2 peocisws vy 60 x 10^3 fibers of polypropylene.



The extracorporeal circuit for LFPPV-$ECCO_2R$.


VENTILATOR
IN
EX
O_2
PEEP
VENTILATORY MANAGEMENT
2-4 BPM
PRESSURE LIMITED VENTILATION (35 - 40 cm H_2O)
APNEIC OXYGENATION BETWEEN BREATHS
PEEP TO MAINTAIN LUNG INFLATION
INSP
INSP
APNEIC OXYGENATION
P cm H_2O
35
15
2 SEC
18 SEC
2 SEC

Essentials of ventilatory management during LFPPV-$ECCO_2R$.

Figure 2 LFPPV-$ECCO_2R$ Technique (From Pesenti A, et al. Trans Am Soc Artif Intern Organs 1980;26:550).

TASK III ADVANCES IN RESUSCITATION SUPPORT SYSTEMS

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VI. Implantable Sensor

I. Introduction and Cardiopulmonary Resuscitation

It is estimated that one third of all deaths in the U.S.A. are due to ischemic heart disease. One half of these are attributable to acute myocardial infarction (AMI). One half of AMI die suddenly (within one hour of onset), and most of the remainder (annually approximately one half million patients) are admitted to the hospital with AMI.

The mortality rate during hospitalization and during the year following myocardial infarction are approximately 15 and 10 percent respectively, with at least half of the post-hospitalization deaths occurring suddenly before the victim can be returned to the hospital. Thus, sudden death from ischemic heart disease is the most important medical emergency today.

It seems probable that a large number of these deaths can be prevented by prompt, appropriate treatment, which may provide either entry into the emergency medical services (EMS) system or cardiopulmonary support using cardiopulmonary resuscitation (CPR).

The National Conference on Cardiopulmonary Resuscitation (CPR) and Emergency Cardiac Care (ECC) held in September 1979 developed standards and guidelines for CPR and ECC as a revision of the 1973 meeting (1). They describe the life support principles and techniques as basic cardiac life support (BCLS) and advanced cardiac life support (ACLS) (2).

Concerning the survivors of out-of hospital cardiac arrest, it was reported that the survival relates to four factors (3): (1) whether cardiac arrest was witnessed, (2) the cardiac rhythm at the time of arrest, (3) whether or not cardiopulmonary resuscitation (CPR) was initiated by lay bystanders, and (4) speed in arrival time of paramedic unit. In 611 patients with out-of-hospital cardiac arrest, these variables were predictive of outcome (Table 1). Among 22 patients with favorable findings on all four predictive factors, 15 (70%) were discharged alive. This contrasts with only one survivor among 97 patients with all four unfavorable findings. Myerberg et al (4) has also described critical importance of the cardiac arrest rhythm. Among 352 consecutive victims of out-of-hospital cardiac arrest, of 24 patients presenting with ventricular tachycardia (VT), 16 (67%) were discharged alive. When the arrhythmia was ventricular fibrillation (Vf), 55 (23%) recovered. However, when a bradyarrhythmia was the initial mechanism, of 108 patients 9 (8%) were resuscitated and none survived. Another helpful predictor is the heart rate immediately after defibrillation. Only 5% survived when the rate was less than 60 beats/min, and 17% when it ranged from 60 to 100 beats/min; of these 43% were long-term survivors (4).

Improvement in results of resuscitation following out-of-hospital cardiac arrest has been progressive. In the period from 1971 to 1973, overall survival was 14%, whereas from 1973 to 1978, it had increased to 23% (4). At present, the hospital discharge rate from out-of-hospital ventricular fibrillation is up to 30% (5). However, long-range survival has been poor. In a prospective follow-up of 276 resuscitated patients who were discharged alive from the hospital, the probability of remaining alive at 4 years was only 49% (6).

New techniques for CPR included multiple transthoracic pacing devices(8), transesophageal cardiac pacing, and retrograde coronary perfusion.

(1) Multipurpose transthoracic pacing device in emergency (8). This device enables: 1) intracardiac epinephrine or other drug injection, 2) the obtaining of a blood sample for arterial blood gases, and 3) the rapid transthoracic insertion of a temporary pacemaker electrode, all simultaneously via a single myocardial needle insertion. This device has been used clinically in ten patients for the emergency treatment of bradycardia or asystole with hypotension. The results were not satisfying but this technique is expected to be useful if it is combined with cardioverter-defibrillators in the future.

(2) Transesophageal cardiac (atrial) pacing (9).
This technique is still in the research phase. If this is mounted on an esophageal obturator airway (EOA) or esophageal gastric tube airway (EGTA), it will be useful for CPR.

(3) Retrograde coronary venous perfusion.
This is achieved by using a balloon-tipped catheter and roller pump for the resuscitation of acute myocardial infarction.

II. Surgical innovation for cardiopulmonary failure

Introduction of coronary arterial surgeries such as bypass surgery improve substantially the outcome of the coronary arterial disease. Autologous saphenous vein graft or internal mammary arterial graft implantation revolutionalized the treatment of coronary arterial disease and prevented the premature sudden death of patients due to the myocardial infarct. Even though the benefits of this surgery are still discussed among medical colleagues, the contributions of this procedures for heart diseases are difficult to negate. Noninvasive balloon angioplastic procedures are also gaining its popularity. If catastrophic cardiopulmonary failure and diseases lead to this failure can be predictable, certainly preventive surgical procedures will be the most ideal resuscitation support we can provide. Some new surgical procedures which might be beneficial from this point of view will be discussed in this section.

(A) Total reversal of pulmonary circulation

Although primary pulmonary hypertension (PPH) is thought to result from increased resistance to pulmonary blood flow occurring at the level of the small pulmonary arteries and arterioles, the actual cause still remains obscure. Since the pulmonary circulation possesses no valves and the direction of flow is determined by the pressure gradient, blood in the pulmonary circulation theoretically could flow in either direction. If the blood could be made to flow into the pulmonary veins and return to pulmonary arteries, the inflow resistance (pulmonary vein resistance) should be less than usual because the cross sectional area of the veins exceeds that of the arteries.

In the literature, Houle (10) established that gas exchange was possible with reversal of the pulmonary circulation to one lobe of the canine lung. All published reports since that time (11-15) have described reversal of flow performed at the level of either one lobe or else a unilateral lung, with survival times of the animal extending over one year, even though the survival rate was low. The lungs can oxygenate venous blood just as well reversed pulmonary circulation as in normal circulation, the resistance to reversed flow being very similar to that of forward flow. There is, however, controversy regarding the long-term effects on the vasculature, in histology for retrograde pulmonary circulation.

Totally reversed pulmonary circulation technique is also still in the research phase (16). Several approaches that have been tried are discussed below.

1. When the heart of the patient is intact, an intra-atrial septation technique have been utilized that is similar to the Mustard operation in TGA (Transposition of Great Arteries) (Figure 1). In this case the left atrium is divided into two chambers (anterior and posterior) by a baffle. The venous blood is pumped out from the right ventricle into the left atrial posterior chamber via an interposed graft, then retrograde into the pulmonary veins. After oxygenated blood returns to the pulmonary artery, it flows into the left atrial anterior chamber, left ventricle, and finally into the ascending aorta.

2. When the heart has severe damage, a single artificial heart could be utilized combined with totally reversed pulmonary flow (16) (Figure 2). After the left and right ventricles are resected at the atrio-ventricular groove, the remnant left and right atria are sutured to make a common atrial chamber. A blood pump is connected to aorta and pulmonary artery. Venous blood from the venae cavae enters a common atrial chamber and then into the pulmonary veins. After oxygenation, the blood returns to the pulmonary artery, blood pump, and finally ascending aorta. With this technique, various kinds of blood pumps (pulsatile or nonpulsatile) could be used. Since heart-lung transplantation is not indicated for elderly patients over 55 years old, the techniques mentioned above could be applicable to elderly patients in the future.

B. Reversal of the Coronary Flow

The theoretical concept of delivering oxygenated blood to an ischemic myocardium by way of the coronary venous system antedated by many decades (17-18) the present widespread utilization of coronary artery bypass grafting. In earlier studies, coronary sinus retrograde perfusion was performed in order to reverse the coronary flow totally. The results achieved by this procedure were summarized by Beck (17-20) as the Beck II operation, which was applied to 186 patients and was approved to be efficacious in selected patients. However, it has been discarded because of a high mortality rate even by Beck himself and due to the advent of aorto-coronary bypass (direct coronary artery revascularization). The retrograde coronary perfusion technique is currently used as a method of myocardial protection during cardiac operations. Coronary artery bypass grafting is now the procedure of choice as a means of myocardial revascularization, but a group of patients remain who are not candidates for this approach.

These are patients who have:

1) Diffuse atherosclerotic disease and poor run-off,
2) Persistently severe angina pectoris following unsuccessful coronary artery bypass operation.
3) Small coronary arteries found at operation with little likelihood of long-term coronary artery bypass graft patency.

Approximately 12 to 30% of the revascularization candidates fall into this group (21-23).

In elderly patients, calcification of the ascending aorta or coronary atheroma is frequently seen. This fact affects selection of the operative procedure. For example, the proximal anastomosis must then be performed in an unusually high aortic positions or even on the innominate artery and endarterectomies have a tendency to be necessary. Since the venous system is not affected by atheromatous changes, there has been renewed interest in reversing flow in the coronary venous system in order to deliver oxygen and substrate to poorly perfused or ischemic heart muscle selectively. This selective retrograde coronary venous perfusion (SRCVP) has been applied to patients who have the above mentioned diseases, using internal mammary artery-coronary vein anastomosis or saphenous vein bypass grafts from aorta to cardiac vein (24-26). The results seemed to be acceptable and encouraging because symptoms such as anginal pain were relieved and tolerance to physical activity improved. However, long-term observation is needed concerning patency of the anastomosis and graft. This technique would be adopted for elderly patients from the indicative disease, since most of the candidates reported were over 50 years old. Recently SRCVP has been studied by providing temporary support to ischemic myocardium in animal experiments. This assist system consists of a balloon-tipped catheter and pump system (such as a roller pump) (27-28) (Figure 3). Moreover, if this system could be used in conjunction with artificial blood (29-31) and a certain kinds of nutrititional solutions, many ischemic disease patients could be saved.

III. Mechanical circulatory assistance

Recent advancements of pump technology are such that it is possible to resuscitate circulatory or cardiopulmonary failure patients by utilizing various types of circulatory assistance.

Depending on the intended function, there are many types of cardiac prostheses available.

Types of cardiac prostheses

(1) Transient cardiac prosthesis

This group of prosthesis is used to support the temporarily failing natural heart and includes intraoartic balloon pumping, cardiopulmonary bypass, and temporary left ventricular assist or biventricular bypass devices. It is expected in these applications that the failing natural heart will recover within several days to several weeks, after which time the assist device can be removed and the patient's heart would resume its normal function. Since emergency applications of these devices is required, simple implantation and removal is necessary. This group of prostheses is available and routinely used on clinical patients.

(2) Interim cardiac prosthesis

This category of cardiac prosthesis is used on patients waiting for a suitable donor heart for transplantation and contains left, right, biventricular assist devices and the total artificial heart (Figure 4). This device can also be applied to the recipient during the possible rejection crisis of the transplanted heart. It is not necessary that this type of prosthesis be totally implantable since its use is intended for only up to one month. Hence pneumatically actuated devices are suitable for this application.

Currently at least seven implantations of such devices have been performed since the mechanical total artificial heart was implanted in a 47 year-old male patient as a bridge procedure to heart transplantation in 1969 (32-33). The pneumatically driven total artificial heart was implanted in a 61 year-old man for permanent use in 1982 (34-36); five implantations have been performed with three patients still alive (37), and one of these three patients has survived for over one year.

The limiting factor in these applications, however, may be infection, as indicated to date by heart transplantation experiences. Two recent developments perhaps will have an impact on this problem: (1) the availability of cyclosporine A as an immunosuppressive agent, which reduces the necessary dosage of steroids and (2) the introduction of plasmapheresis technology as a means of combating infections. Leukopheresis allows for massive leukocyte infusion for the prevention and treatment of infection in addition to the currently available antibiotic regimens. Other possibilities are also offered by plasmapheresis, since antibodies can be removed quite effectively and hence the presently employed immunosuppressive therapy could be reduced or even eliminated.

(3) Permanent cardiac prosthesis

This group of devices is intended to be totally implantable for up to two years and is still under development.

Development of a totally implantable electrically actuated left ventricular assist device system (LVAS) is now in the preclinical evaluation phase. At least six groups (Table 2) in the world are trying to develop this system. The LVAS consists of a blood pump, energy converter, variable volume compensation device, internal battery, transcutaneous energy transmission system, external battery and a diagnostic system (Figure 5,6,7). System reliability has been assured in animal experiment for up to seven months. Some of these will be available by the end of 1987 (38). After that, clinical trials will be initiated.

As another totally implantable LVAS, thermal engine ventricular assist programs (39) are currently being pursued by two groups in the USA and one group in the USSR. This system is driven by a Stirling cycle engine and uses electrically heated, morten salt as a source of energy. Utilization of plutonium 238 as a power source would make a system operative for at least 10 years, but the current social climate in the western hemisphere is not in favor of such an atomic energy application. In vivo animal experiments have been continuing to evaluate the system performance (Figure 8).

The development of a variable volume compensation device (compliance chamber) (40) is essential for both the electrical and thermal LVAS. Durability of this device has been demonstrated for up to 2 years in animal experiments. Prevention of gas leakage and improved gas refill methods are problems that remain to be solved.

A completely implantable total artificial heart (Figure 9,10) will be available for temporary application by 1991 and permanently by 1995 on the basis of the techniques and components learned from the totally implantable LVAS development (38). Currently at least six groups in the world are working toward this goal (41).

These cardiac prostheses are particularly useful for the elderly, since patients 55 years and older are excluded as candidates for heart transplantation.

IV. New Therapy for Malignant Tachyarrhythmias

There are three currently available techniques for the purpose of terminating ventricular tachycardia and fibrillation. They are as follows (42):

1. high energy defibrillation

2. antitachycardial pacing

3. low energy cardioversion

The three techniques have many advantages in that these devices can be implanted by relatively minor surgical procedures, can control ventricular tachyarrhythmia resistant to usual drug treatment, and can eliminate the side effects of drugs. These techniques are more suitable for the elderly patients who are suffering from recurrent life-threatening ventricular tachycardia (VT) and fibrillation (VF).

1. Defibrillators

Implantation of a defibrillator has become a routine procedure to treat malignant ventricular tachyarrhythmias. Since the first automatic defibrillator was implanted in a 57 year-old-woman suffering from recurrent life-threatening ventricular arrhythmias unresponsive to conventional drug therapy in February 1980 (43), over 500 defibrillators have been implanted. The automatic implantable defibrillator (AID) (manufactured by INTEC Systems, Inc., Pittsburgh, PA., USA) is an electronic device designed to monitor cardiac rhythm continuously, to identify ventricular tachycardia and fibrillation accurately, and then to deliver high energies in the range of 25 to 30 joules promptly when such arrhythmias occur (Figure 11).

Results of clinical trials demonstrated that this device was suitable for successful arrhythmia termination in a great majority of patients at risk for sustained ventricular tachycardia and fibrillation. Echt (44) reported that the AID could reduce the one year sudden death rate from 25 to 30% to as low as 1.8% in patients who have already experienced episodes of sustained ventricular tachycardia and fibrillation. The majority of recipients of an AID have coronary artery disease or a myocardiopathy as a basic disease (Table 3) and have poor left ventricular function (ejection fraction below 30% and average age around 55 years old). Although endocardial mapping and use of excision or cryoablation can achieve control of ventricular tachycardia in selected patients, the procedure has a high operative mortality in the range of 9 to 20%) and is not well suited to patients with polymorphic VT or Vf, multiple morphologies at VT and/or poor left ventricular function (45).

It is probable that defibrillator implantation will be the primary therapy for VT and VF in place of drug therapy. Since the surgical risk and incidence of the side effects of antiarrhythmic drugs are much higher in elderly patients than in younger patients, defibrillator implantation seems to be the primary therapy of choice.

2. Antitachycardia pacemaker

Several kinds of antitachycardia pacemakers have been developed for automatic termination of ventricular tachycardia and fibrillation and have undergone clinical trails (46-50). Currently available devices are shown in Table 4. Most of the patients implanted with these antitachycardia pacemakers are 50+ years old. Ventricular tachycardia termination may be accomplished by single, double or triple extrastimuli, burst, or overdrive suppression. The antitachycardia pacemaker has the advantage that low energy consumption is required to terminate VT, and therefore the generator can be considerably smaller than those required for low energy cardioversion and defibrillation. The termination of the ventricular tachycardia can be achieved with no discomfort to the patient. An other advantage is that only minor surgical procedures are required for insertion.

3. Low energy cardioverter

One other available technique for automatic termination of ventricular tachyarrhythmias is low energy cardioversion (less than 5 joules). A low energy cardioverter consists of a smaller generator (Figure 12) and a fully transvenous lead system that can be inserted with a relatively minor surgical procedure. This device (Medtronic Model 7210) has been applied to seven patients to date (mean 64 years old mean, range 56-68 years) (51).

The antitachycardia pacemaker and cardioverter needs a defibrillator as a back up system to prevent several harmful complications such as acceleration. On the other hand the high energy produced by the defibrillator is not always necessary to terminate defibrillation. Therefore, an ideal automatic electronic tachycardia terminating device should combine antitachycardia pacemaking, low energy cardioversion, and backup higher energy defibrillation. It should be fully programmable between these three modes of tachyarrhythmia termination and use various combinations of these technologies. The ideal system should use transvenous electrode system and the automatic arrhythmia detection algorithms based not only on a patient's rhythm but also on the physiological consequences of the arrhythmia.

V. Implantable cardiac pacemaker

A permanent pacemaker implantation is the routine treatment for arrhythmias. The implantable pacing system consists of a generator and the flexible conductive lead (electrode).

1. Generator (battery)

The life span of the generator has been extended for up to 10 years by improvements in the energy source from a zinc-mercuric oxide electrochemical cell to a lithium iodide cell (Figure 13). However, replacement of the battery still cannot be avoided. A telemetrically rechargeable generator is expected to be developed for this purpose by modifying a transcutaneous energy transmission system which is one of the main components of totally implantable LVAS funded by the NIH. All transcutaneous energy transformers utilize a magnetic flux linkage between a primary and a secondary coil to transmit power: they have the primary transformer outside of the body while the secondary is totally implanted (52-53).

A different approach solving this problem is nuclear pacing which is powered by the isotope plutonium 238 (Table 5). Parsonnet (54) reported higher reliability, superior performance and safety of a nuclear pacing system. Actual survival at 10 years was 92%, meeting the expected performance goal of 90% (Fig 13). The common cause of replacement was an inappropriate pacing mode (fixed rate pacing mode). The causes of death of 25 of the 131 patients was not attributable to failure of the pacing system. This successful result suggests that the combination of a radioisotopic power source with a multiprogrammable dual-chamber pacemaker could at least provide a physiologic pacing system that would last the lifetime of virtually every patient. Its use is not permitted now due to sociological reasons.

2. Lead (electrode) system

Breaking and dislodgement of the lead wire and tip are the usual cause of the pacing or sensing failure. Silicone was the main material used for the pacing lead, but recently polyurethane or Biomer-like segmented polyether polyurethane leads have been utilized clinically or studied in animal experiments. To prevent dislodgement of the lead, the shape of the lead tip has been designed to anchor well into the trabeculation of the ventricle and atrial appendage.

An implantable leadless pacing system has been developed to eliminate lead-related complications, however these are still in the research phase. A leadless pacemaker consists of completely separate transmitter and receiver modules. The transmitter contains a battery, a pulse timing circuit and a oscillator driving a tuned circular coil. The receiver module contains a second tuned circular coil and a peak-to-peak detector circuit connected across the bipolar screw-in electrode on which the module is built. This system uses electromagnetic induction to transmit electrical impulses to the heart in place of the flexible lead. An asynchronous mode, leadless pacemaker and leadless ventricular inhibitory pacemaker have been designed and tested in animal experiments.

3. Multiprogrammable pacemaker (physiological pacing)

"Pacemaker Syndrome", which was first described by Mitsui (55), is characterized by palpitations, a feeling of malaise, vasomotor problems, and sometimes anginal pain. These symptoms may be attributed to poor circulatory adaptation to the pacing rate, but the essential element of the syndrome is the interruption of atrio-ventricular sequence (A-V synchrony) in the demand type VVI pacemaker, resulting in AV valve dysfunction and drop in cardiac output. Recently physiologic pacing systems that can activate the atrium, reestablish AV synchrony, and result in better patient comfort and exercise tolerance have been developed as a DVI (A-V sequential) pacemaker or a dual chamber (VDD, DDD) pacemaker (Table 6). Since A-V synchrony can increase cardiac output by 20% these pacemakers are very effective in patients with *normal* sinus node function during daily activity and exercise. However these are contraindicated in patients with sinus node dysfunction, especially with sinus bradycardia or atrial fibrillation.

In an attempt to find a method of providing rate-responsive pacing to those patients with sinus node dysfunction, some investigators have turned to other indicators of physiologic demand beside the atrium. This physiological responsive pacing can be defined as pacing to optimize cardiac output to meet metabolic needs in the absence of normal physiological control. Control is achieved by sensing some physiological variables that are correlated to actual physiologic need, hence increasing (or decreasing) paced heart rate and cardiac output.

a) Temperature (56, 57) - A thermister is mounted on a lead in the right ventricle to measure mixed venous blood temperature. Temperature increases during exercise because of the exercising muscles and the concomitant body core temperature increase. Increasing temperature produces a higher paced rate. This is in the research phase (Figure 14).

b) QT interval (58) - A right ventricular unipolar-like electrode is used to detect the repolarization, (T-wave) subsequent to the pacemaker stimulus. QT interval normally shortens due to changing sympathetic tone and circulating catecholamines. A shorter QT interval produces a higher paced rate.

This development was realized with the TX_1 pacemaker, which is based on the Vitatron DPG generator (Vitatron Medical BV, Dieren, The Netherlands), and three patients have received the TX_1 pacemaker.

c) Respiratory rate (59,60) - A separate lead subcutaneously transversing the thorax is used to measure electrical impedance changes due to changing lung volume. The average sensed respiratory rate is used to control the heart rate. Higher respiratory rates produce a higher pacing rate.

This rate responsive respiratory-dependent pacemaker (Biotec S.P.A., Bologna, Italy) was implanted in 22 patients: mean age 65, range 22-88 years. Nineteen of these patients received respiratory-dependent ventricular pacing (VVI-RD) and 3 patients received respiratory-dependent atrial pacing (AAI-RD) (Figure 15).

d) Oxygen saturation (61) - An optical detector on a lead (fiber optic catheter) in the right ventricle measures the mixed venous oxygen saturation (Figure 16). As mixed venous oxygen saturation diminishes, the pacing rate increases.

This technique is also being evaluated in

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patients implanted with permanent pacemakers.

e) pH (62) - A membrane pH electrode near the distal end of the right ventricle lead senses the pH which is proportional to the concentration of carbon dioxide generated by exercising. As the pH diminishes, the pacing rate increases.

Seven devices were implanted in patients from 1977 to 1979. The resultant potential problems derived from biocompatibility of the electrode and tissue growth around the electrode tip.

f) Body activity (63) - An accelerometer-like sensor in the pacemaker senses whole body motion and some secondary local muscle motion. As body activity increases, the sensor signal likewise increases, and the pacing rate.

g) Stroke volume (64) - By measuring changes in intracavitary impedance, this sensor is capable of detecting relatively small changes in stroke volume.

h) Preload (end-diastolic pressure) and contractility (dpldt) (65) - An intracardiac pressure transducer could be used to assess alterations in preload and contractility. Such data could be employed by a rate responsive pacemaker. These are still in the research phase.

VI. Implantable Sensors

The development of various implantable devices such as cardiac prostheses, pacemakers, cardioverters, and defibrillators have created an increasing need for implantable sensors (65) that could be incorporated into such systems to control them more physiologically.

1. Physical transducers

Physical transducers may be used to measure pressure, flow, acceleration, velocity, position etc. Implantable ultrasonic and electromagentic flow transducers have been developed over the last twenty years. These have been implanted for various periods of time and are commercially available. Both piezoresistive and capacitive sensors have been studied for implantation purposes as pressure transducers. Although packaging techniques to protect the lead wires still remains a problem, both sensors can be implanted in the body with relatively good stability. Since the maximum measurable pressure of these sensors depend on the diaphragm thickness, a silicon diaphragm sensor could be used to measure force, stress, strain, sound and vibration with some modification of the diaphragm. Miniature silicon acceleration devices have been developed. Integration of the acceleration could yield velocity information, and then with a second integration, obtain an indication of position.

Several miniaturized solid state flow sensors used temperature gradients and thermal loss as a measure of flow velocity.

2. Chemical Sensors

Ion selective electrodes have been used for many years. There are two important new developments in this field. One is an ion sensitive field effect transistor (ISFET) and the other is a fiber optic sensor. The ISFET is made basically for pH measurement, but can also be used as a specific ion sensor, for K+, Na+, Ca++, etc, when combined with a special ion selective membrane. The ISFET can also be used to measure glucose, lactate, urea, etc. by immobilizing enzymes onto the membrane.

The fiber optic sensor is a device which utilizes the difference in absorption of the light wavelength, by the use of certain dye. pH, pO2, pCO_2, alcohol, and lactate sensors are reported in the literature.

In spite of many efforts devoted for the development of reliable sensors, currently it is quite a disappointment for the availability of clinically reliable sensors. Many years effort are necessary to achieve this goal.

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LEGEND OF TABLES

Table 1	Outcome among 611 patients with out-of-hospital cardiac arrest.
Table 2	Long-term electric left ventricular assist systems under development in the United States.
Table 3	Characteristics of 78 consecutive patients selected for AICD implantation.
Table 4	Currently available antitachycardia pacemaker.
Table 5	List of pacemakers implanted, inclusive dates of implants (first and last of series), number out of service and deaths, percent of original implants still in service, and age of the oldest still in service.
Table 6	Available DDD pacemakers

Table 1 Outcome Among 611 Patients With

Out-of-Hospital Cardiac Arrest

Event Witnessed	Number of Patients	Discharged Alive(%)
+	380	28*
-	231	3
Arrythmia of cardiac arrest		
VT or VF	389	23*
Asystole	222	3
Bystander-Initiated CPR		
+	168	32*
-	443	14
Response Time (min)		
4.0	39	56
4.0-8.0	139	35
8.0	186	17

*p 0.01

(From: Eisenberg M., et al. JAMA 1981;246:50)

Table 2 *Long-term electric left ventricular assist systems under development in the United States*

Institution	Corporation	Type/description energy converter	Blood contacting surface	Valve type	Pump location
The Pennsylvania State University	Sarns, Inc.	*Electromechanical*/low-speed reversing motor drives cam or high-speed reversing motor drives roller screw	Smooth Biomer	Bjork-Shiley	Subdiaphragmatic
Children's Hospital Medical Center (Boston)	Thermedics, Inc.	*Electromechanical*/low-speed motor drives cam	Textured Biomer diaphragm within a powered titanium surface	Bovine pericardium	Subdiaphragmatic
Texas Heart Institute (Houston)	Gould, Inc.	*Electromechanical*/high-speed motor and gears drive cam	Textured Biomer diaphragm within a powered titanium surface	Porcine xenograft	Subdiaphragmatic
Stanford University	Novacor Medical	*Electromechanical*/solenoid energizes two opposite pusher-plates	Smooth Biomer	Porcine xenograft	Subdiaphragmatic
Massachusetts General Hospital (Boston)	Abiomed	*Electrohydraulic*/motor-driven turbine pressurizes silicone fluid that compresses blood sac	Smooth Angioflex	Human Dura mater	Intrathoracic
Cleveland Clinic Foundation	Nimbus, Inc.	*Electrohydraulic*/motor-driven gear pump pressurizes silicone fluid that moves pusher plate	Biolized gelatin		

(From: Gaines W.E., et al. Heart Transplantation 1984;3:323-328.)

Table 3 Characteristics of 78 Consecutive Patients Selected for AICD Implantation

Males/Females:	60/18
Mean Age (range):	54 yrs. (16-74)
Primary Cardiovascular Diagnoses	
coronary artery disease:	59 (76%)
primary cardiomyopathy:	18 (23%)
prolonged QT syndrome:	1 (1%)
Ejection Fraction (mean):	.32
Previously Failed Antiarrhythmia Drugs (mean):	4.5
Previous Episodes of Sudden Cardiac Death (mean):	3.5
Previous Cardiovascular Surgery	
coronary artery bypass:	13
myectomy:	1
pacemakers:	10

(From: Reid, P.R., et al. PACE 1984;7:1338-1344).

Table 4 Currently Available Antitachycardia Pacemaker

MANUFACTURER/MODEL	MODE
Telectronics/Pasar	Extrastimuli, Burst
Telectronics (Optima-MP)	Dual Demand
Intermedics (Cybertach)	Burst
Medtronic (Symbios)	Burst, Dual Demand
Medtronics (5998)	Burst (Externally triggered)
MSiemens-Elema (668)	Dual Demand
Cordia (Omni-Orthocor)	Burst, Extrastimuli (externally triggered)

Table 5

List of pacemakers implanted, inclusive dates of implants (first and last of series), number out of service and deaths, percent of original implants still in service, and age of the oldest unit still in service.

Model	Number Implanted	Dates of Inclusive Implant	Out of Service (Deaths)	% In Service (Excluding Deaths)	Oldest Unit (Months)
Cordis 184 A, B	58	10/29/74 to 1/1/83	15 (8)	86% (43/50)	91
Medtronic 9000A	37	8/3/73 to 12/8/76	21 (8)	55% (16/29)	114
Numec/Arco	36	4/9/73 to 1/27/75	17 (7)	65% (19/29)	120
Coratomic C-100	20	11/7/74 to 11/19/80	8 (2)	67% (12/18)	100
Totals	151	4/9/73 to 1/1/83	61 (25)	71% (90/126)	

(From: Parsonnet V., et al: PACE 1984;7:90-95).

TABLE 6 AVAILABLE DDD PACEMAKERS

MANUFACTURER/MODEL	PACING MODE			
MEDTRONIC/VERSATRAX 7000	DDD	DVI	VVI	
MEDTRONIC/VERSATRAX 7000A-235	DDD	DVI	VVI	
MEDTRONIC/SYMBIOS 7007/7008	DDD	DDO	DVI	
INTERMEDICS/COSMOS 283-01	DDD	VVT	OOO	
	VDD	VPP	DVO	
	AOO	AAI	DOO	AAT
TELECTRONICS/AUTIMA 2251	DDD	DOO	DVI	VOO
	VDD	VVI		
TELECTRONICS/AUTIMA II 2291	DDD	DOO	DVI	VOO
	VDD	VVI		
PACESETTER AFP	DDD	VVT	DDI	DVI
	AOO	DDX	VDD	AAI
	OFF	VVI	AAT	VOO
	DOO			
	(DDD with PVC detector on)			
CPI/DELTA	DDD	DOO	ATT	
	VDD	VVT	AAI	
	VAT	VVI	AOO	
	DVI	VOO		
CORDIS/GEMINI 415-A	DDD	VVT	VVI	
	VDD	AAI		
CORDIS/SEQUICOR 233F	DDD	VDD	DVI	VVI

(pacing mode is described according to three-letter code).

LEGEND OF FIGURES

Figure 1a	Intra-atrial septation technique to reverse the pulmonary circulation.
Figure 1b	Intra-atrial septation technique to reverse the pulmonary circulation.
Figure 2	One pump TAH with reversed pulmonary flow.
Figure 3	Schematic diagram of the diastolic synchronized retroperfusion experimental system. Arterial blood is shunted from a peripheral artery to the diastolic synchronized retroperfusion (D.S.R.) catheter located in the coronary (C) sinus. Diastolic synchronized retroperfusion is achieved by means of an air-blood unit, which is actuated by an electropneumatic console.
Figure 4a	(Jarvik 7) Diaphragm type total artificial heart.
Figure 4b	Dual pusher-plate type total artificial heart (Cleveland Clinic).
Figure 5a	Proposed anatomical locations of E3C implantable components of Nimbus-Cleveland Clinic ventricular assist system.
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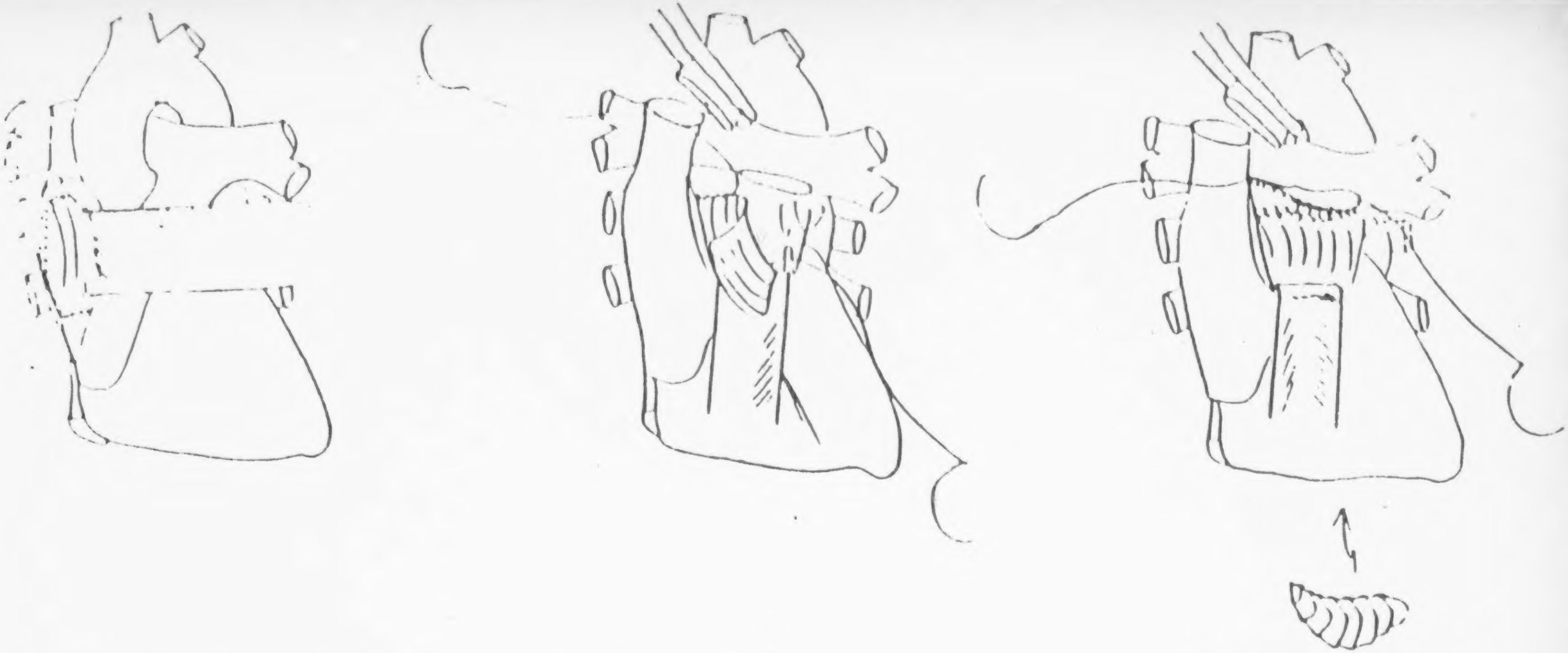
Figure 10	The Pennsylvania State University roller screw drive total artificial heart.
Figure 11	The automatic implantable cardioverter-defibrillator with, left to right, its superior vena cava, bipolar right ventricular, and apical patch electrodes.
Figure 12	Picture of cardioverter and lead in surgeon's gloved hand.

Figure 13 Acturial survival of pulse generators as a function of power scruce. Note the 80 percent survival of lithium batteries at 90 months compared with the previously used mercury-zinc batteries.

Figure 14 The implantable temperature-controlled pacemaker system. The microcomputer-based pulse generator measures temperature from a thermistor in the lead and delivers stimuli through the pacing electrode. Whlie exercise is detected from right ventricular temperature, the microcontroller increases the ventricular pacing rate. The percutaneous connector allows direct recording of the ventricular electrogram and temperature.

Figure 15 Diagram of followup. Nineteen patients received rate responsive respiratory-dependent ventricular pacing (VVI-RD) and 3 patients received rate responsive respiratory-dependent atrial pacing (AAI-RD).

Figure 16 Cross-section through the S -sensor.

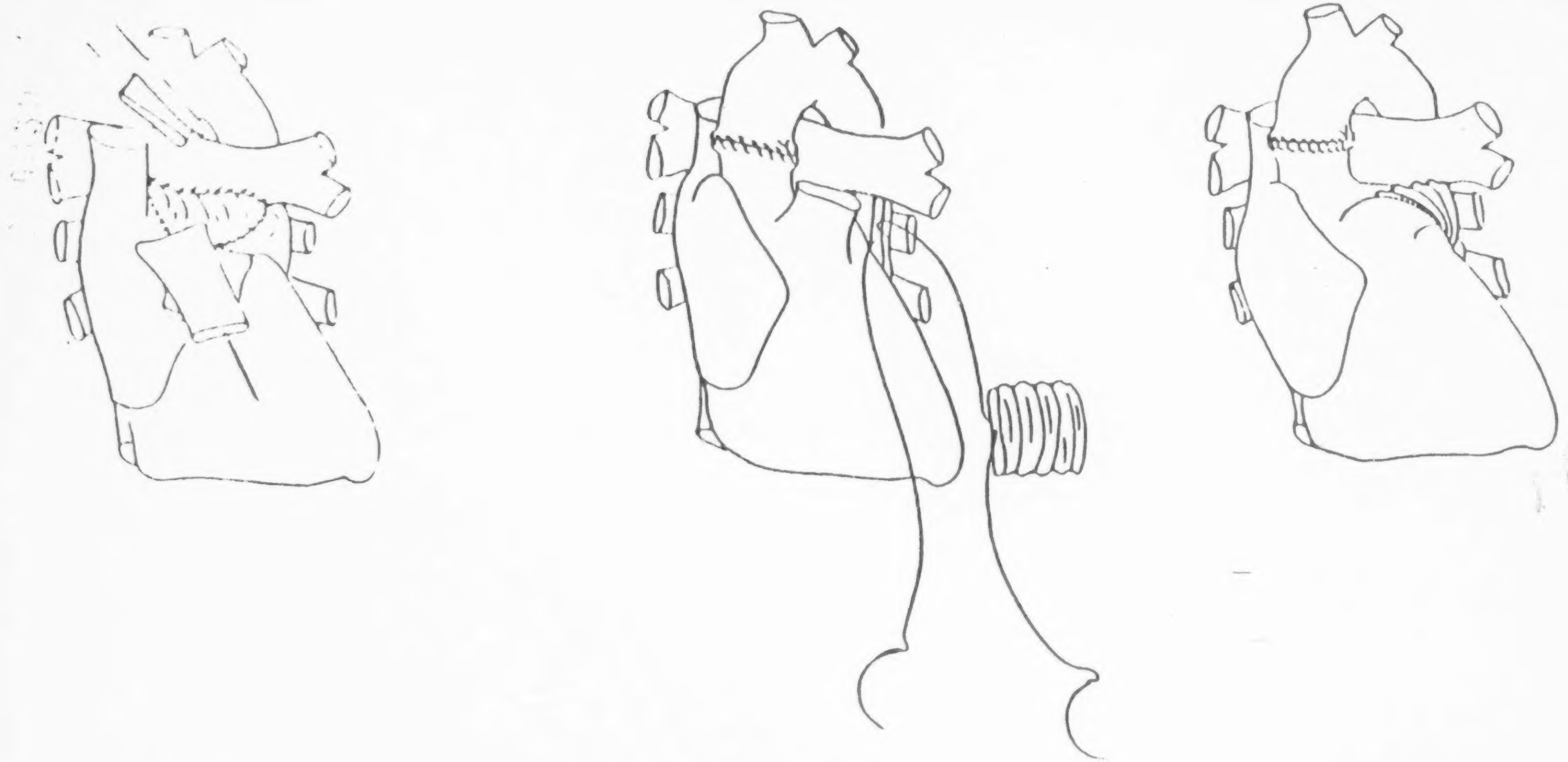


1. Left atrium is opened and a Dacron baffle is sutured over the orifices of pulmonary veins.

2. After division of aorta and pulmonary artery, left atrial roof is opened and suturing of the baffle is completed. Now, both the orifices of all pulmonary veins and the aperture of the left atrial appendage are excluded from the functional left atrium.

3. After extending the opening in the pulmonary artery bifurcation the back wall of the pulmonary artery is sutured to the inferior edge of the roof of the left atrium. A patch of Dacron is required anteriorly.

Fig 1(a) Intra-atrial septation technique to reverse the pulmonary circulation.

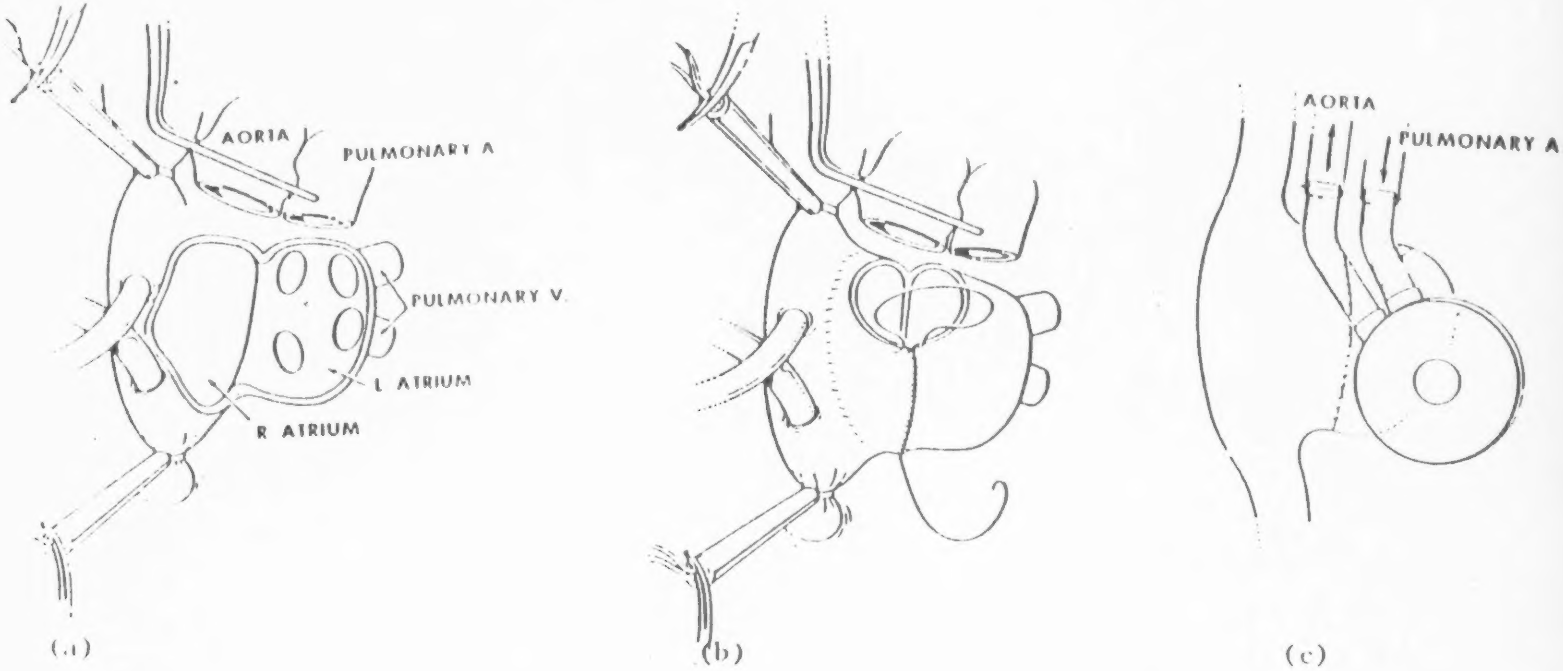


4. The pulmonary artery-to-left atrial connection is now completed.

5. Following repair of the aorta, the left atrial appendage is anastomosed to a Dacron graft.

6. The proximal end of the graft is anastomosed to the stump of the pulmonary artery, permitting blood to flow into the pulmonary veins, under the baffle. Return from the lungs is via the pulmonary artery then into the left atrium under the patch.

Figure 1(b) Intra-atrial septation technique to reverse the pulmonary circulation



(a) (b) (c)

Figure 2 One pump TAH with reversed pulmonary flow

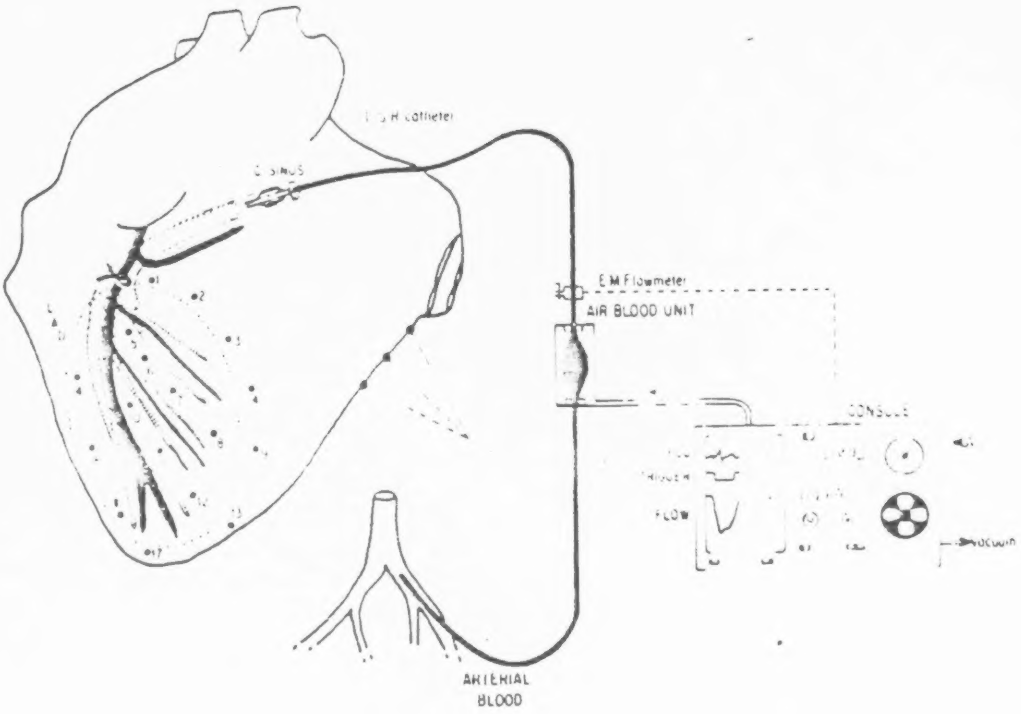


Figure 3 Schematic diagram of the diastolic synchronized retroperfusion experimental system. Arterial blood is shunted from a peripheral artery to the diastolic synchronized retroperfusion (D.S.R.) catheter located in the coronary (C) sinus. Diastolic synchronized retroperfusion is achieved by means of an air-blood unit, which is actuated by an electropneumatic console.

(From Berdeaux A., et al. Am J Cardiol 1981;47:1033-1040).

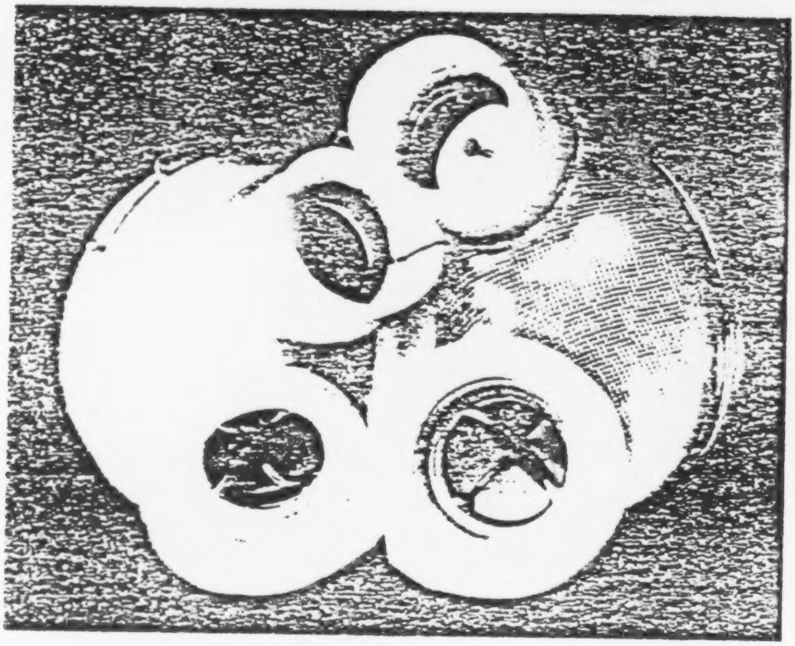


Figure 4(a) (Jarvick 7) Diaphragm type total artificial heart

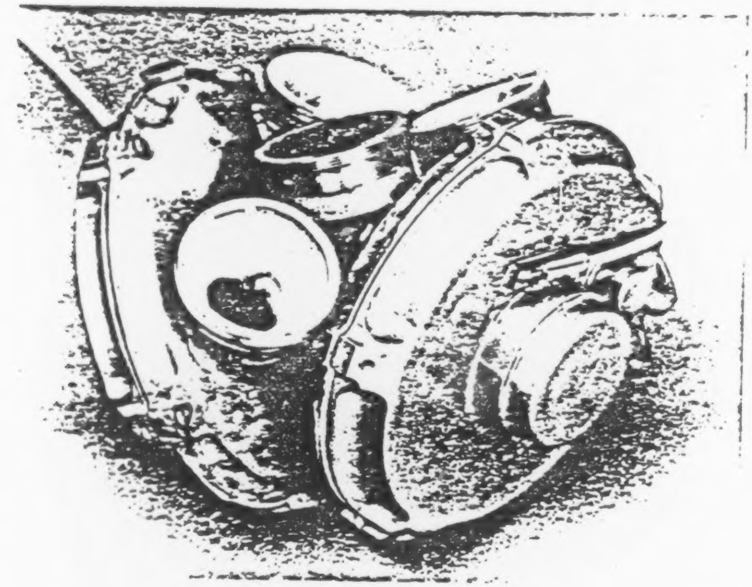


Figure 4(b) Dual Pusher-Plate type Total Artificial Heart (Cleveland Clinic)

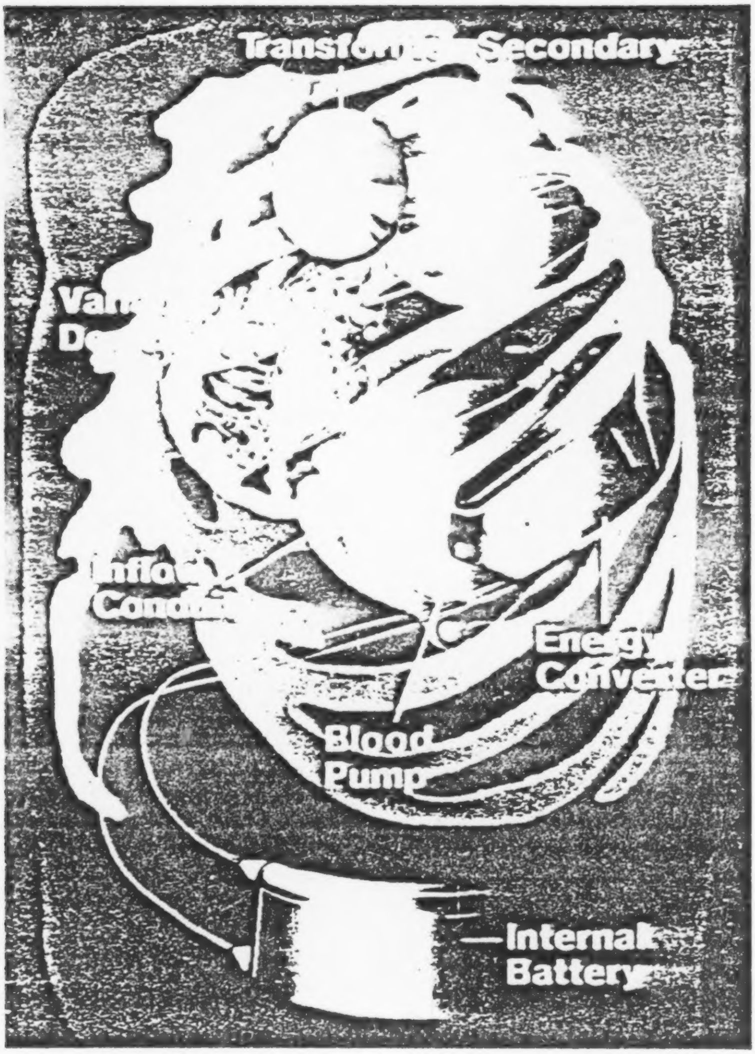


Figure 5(a)

Proposed anatomical locations of E3C implantable components of Nimbus-Cleveland Clinic ventricular assist system.

Figure 5(b) Pump-actuator components of the above mentioned system.

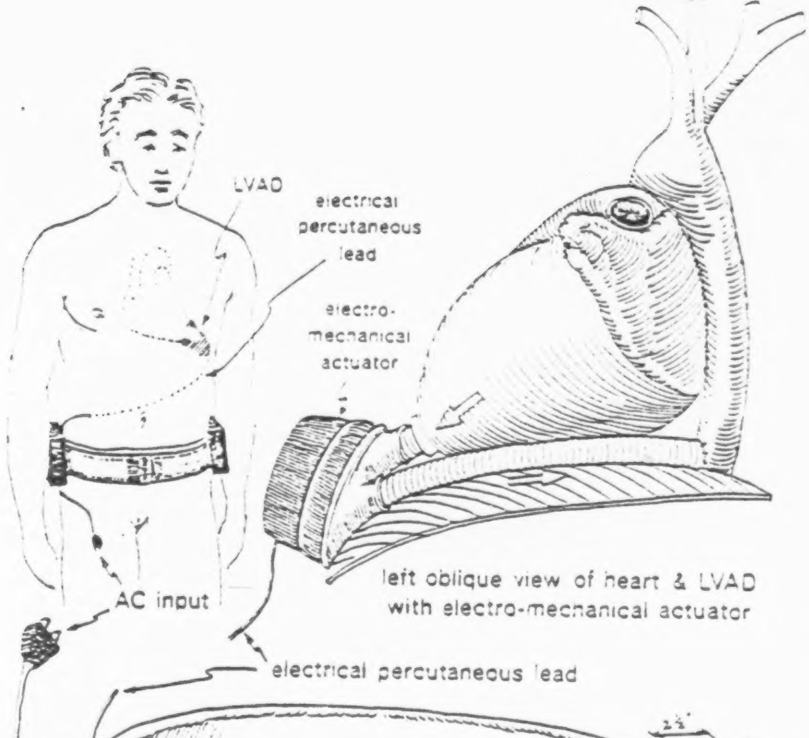

LVAD
electrical percutaneous lead
electro-mechanical actuator
left oblique view of heart & LVAD with electro-mechanical actuator
AC input
electrical percutaneous lead
electrical controls
battery pack

Figure 6 Schematic representation, showing the complete Novacor-Stanford VAS, and the anatomic location and relationship of subsystems.

(From Altieri F.D. Artif Organs 1983;7:5-20).

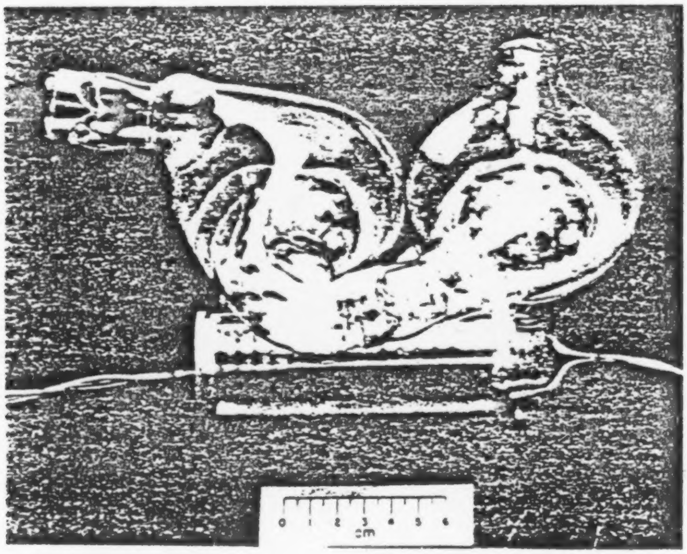


Figure 7 Dual chamber pump. The cylinder tucked under the pumping chambers houses the hydraulic drive unit. (Abiomed, Danvers, Mass.)

(From Singh P.I., et al. Trans Am Soc Artif Intern Organs 1982;28:117-122).

566

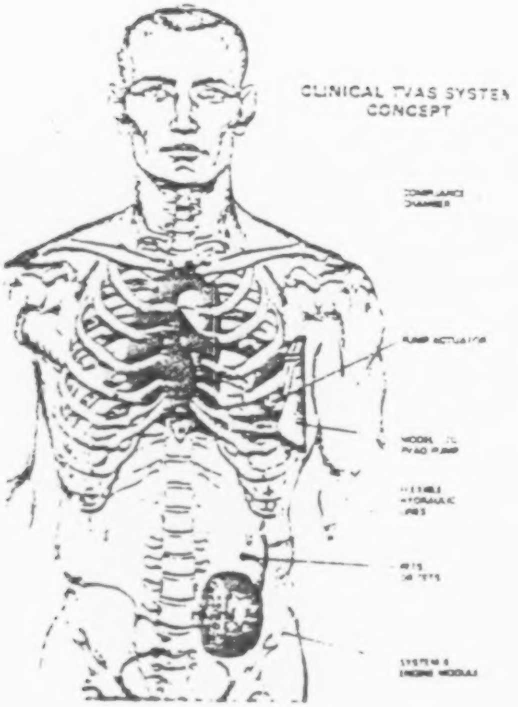


Figure 8 Locations of the pump-actuator and the engine module.
System 8 developed by Cleveland Clinic, University of Washington and Whalen Biomedical.

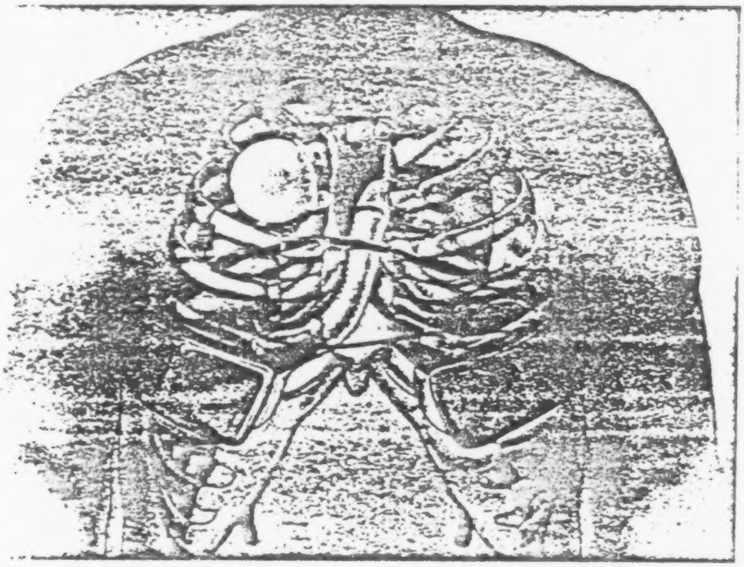


Figure 9 Completely implantable TAH system proposed by Cleveland Clinic and Nimbus, Inc.

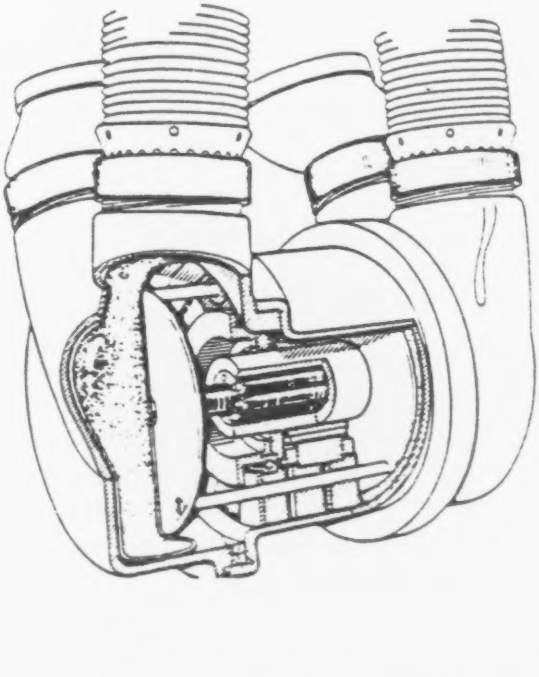


Figure 10 The Pennsylvania State University roller screw drive total artificial heart.

(From Rosenberg G., et al: Trans Am Soc Artif Intern Organs 1982;28:123-126.

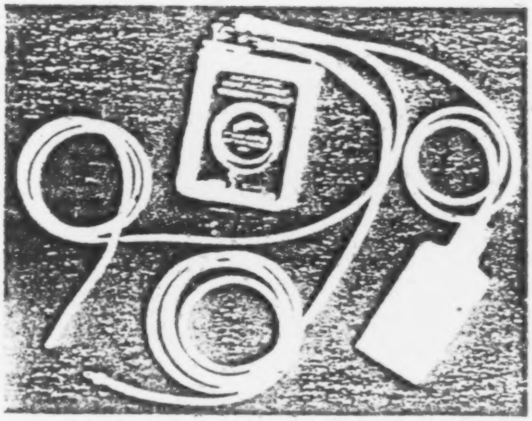


Figure 11 The automatic implantable cardioverter-defibrillator with, left to right, its superior vena cava, bipolar right ventricular, and apical patch electrodes.

(From Mirowski M., et al. PACE 1984;7:534-540).

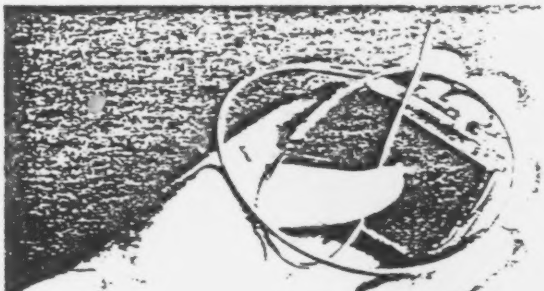


Figure 12 Picture of cardioverter and lead in surgeon's gloved hand.

(From Zipes D.P., et al. PACE 1984;7:1325-1330).

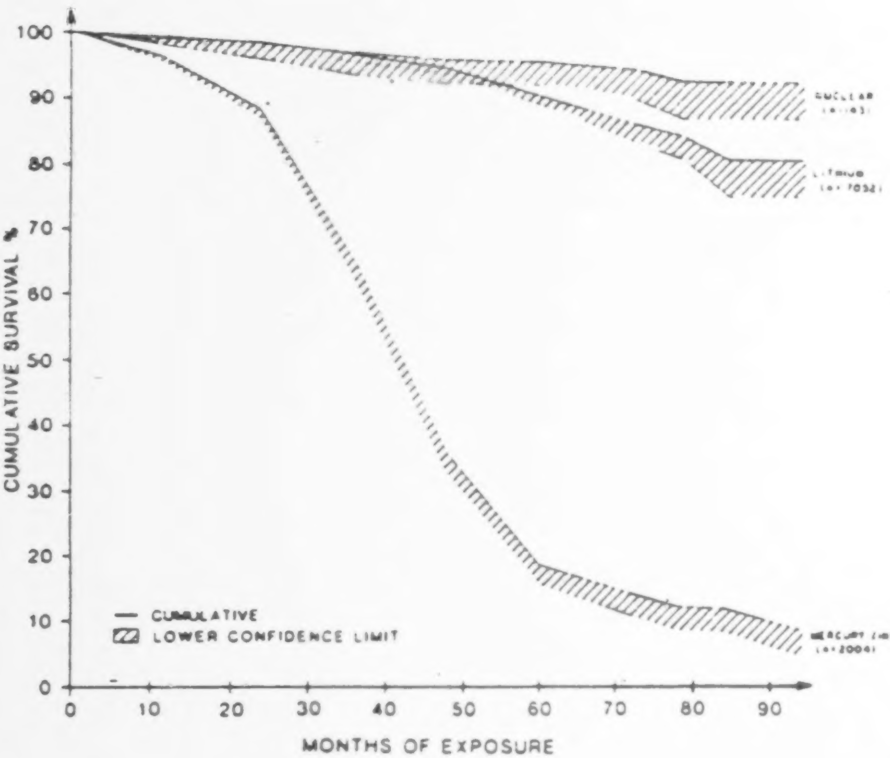


Figure 13 Acturial survival of pulse generators as a function of power source. Note the 80 percent survival of lithium batteries at 90 months compared with the previously used mercury-zinc batteries.

(From Personnet V., et al. PACE 1984;7:90-95).

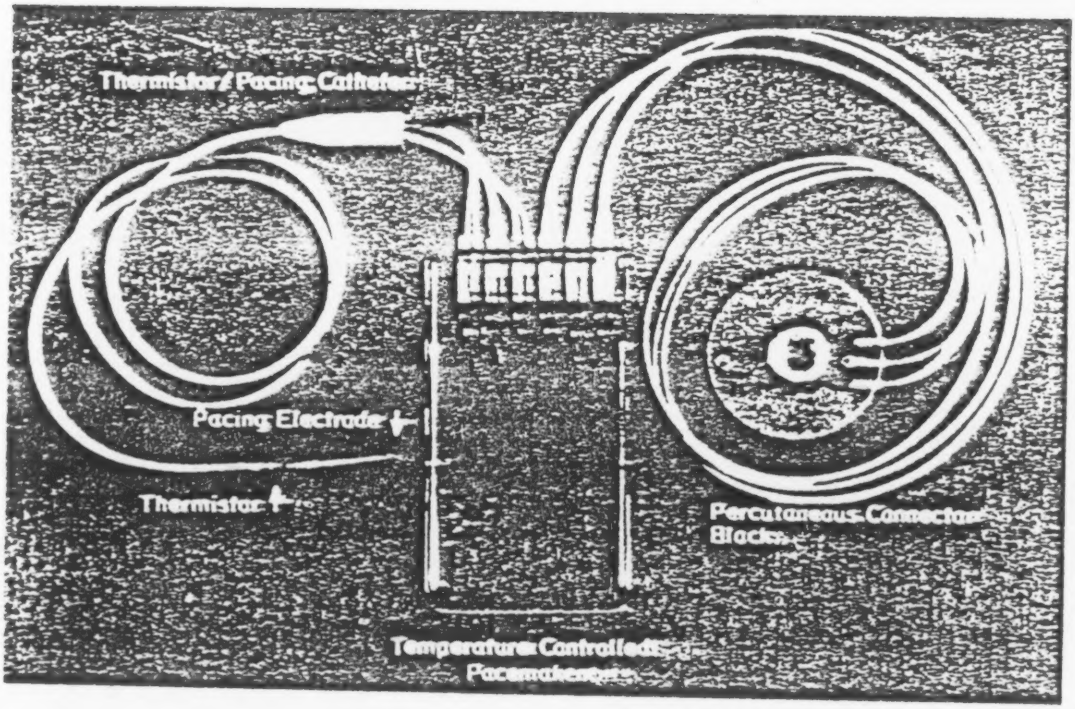

Thermistor/Pacing Catheter
Pacing Electrode
Thermistor
Percutaneous Connector Block
Temperature Controlled Pacemaker

Figure 14 The implantable temperature-controlled pacemaker system. The microcomputer-based pulse generator measures temperature from a thermistor in the lead and delivers stimuli through the pacing electrode. While exercise is detected from right ventricular temperature, the microcontroller increases the ventricular pacing rate. The percutaneous connector allows direct recording of the ventricular electrogram and temperature.

(From Fearnot N.E., et al. PACE 1984;7:1240-1245).

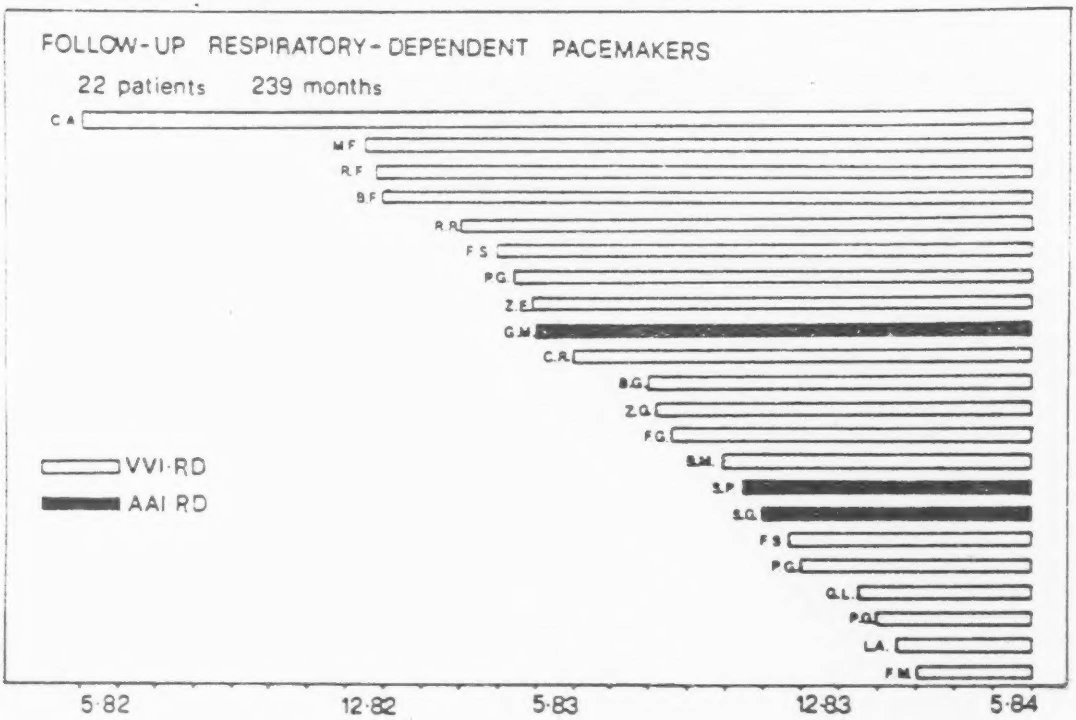


Figure 15 Diagram of followup. Nineteen patients received rate responsive respiratory-dependent ventricular pacing (VVI-RD) and 3 patients received rate responsive respiratory-dependent atrial pacing (AAI-RD).

(From Rossi P., et al. PACE 1984;7:1246-1256).

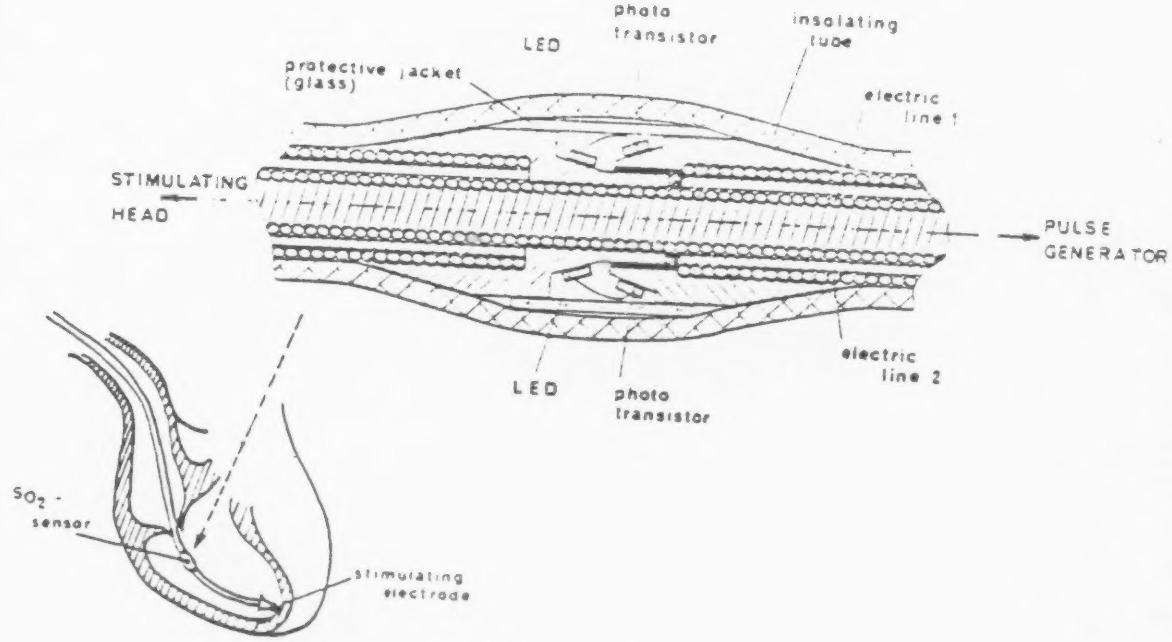


Figure 16 Cross-section through the S_{O_2}-sensor.

(From Wirtzfeld A., et al. PACE 1983;6:494-497).

TASK IV: ADVANCES IN NUTRITIONAL SUPPORT TECHNOLOGY

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TASK IV: ADVANCES IN NUTRITIONAL SUPPORT TECHNOLOGY

I. Introduction

II. Nutritional Support
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    B. Parental nutrition
    C. Enteral nutrition

III. Therapeutic Apheresis

IV. Method of Plasma Separation

V. Therapeutic Plasmapheresis

VI. Plasma Treatment
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TASK IV: ADVANCES IN NUTRITIONAL SUPPORT TECHNOLOGY

I. INTRODUCTION

From the report of the Bureau of Census in 1984, the population and ratio of the elderly in the United States has been increasing(1). In 1960, the population of the elderly over 65 years old was 16.5 million and the ratio was 8.0% of the total population. In 1982, however, the population and the ratio had increased to 25.2 million and 11.2%, respectively. With the increase of the elderly, the number of deaths by diseases, as well as by malnutrition, have also been increasing. More than 50,000 hospitalized patients die in the United States yearly because of nutritional deficiency. Furthermore, it is estimated that nutritional deficiency affects more or less 500,000 yearly in their struggle to recover from a malnutritional state. Recently, the rate of malnutrition has risen to 56% - 85% at various nursing homes. Recent progress, however, in nutritional supporting technologies has provided the improvement of the nutritional state of patients with critical states such as a serious burns, cancer, pre and post major surgery and sepsis. For the treatment of the elderly, however, special considerations have to be paid to their underlying metabolic and immunologic disorders. For example, even with a human considered to be healthy, normal values of plasma fibrinogen levels increase with age (Table I)(2). In addition, the common diseases in the elderly such as cardiovascular disease, diabetes mellitus, cancer and chronic liver disease are greatly related to the malfunction of the immmuno-metabolic system.

Thus, conditions of the elderly or of their nutritional state are referable to the changes in metabolism that occurs with aging. In other words, the correction of abnormal metabolism of the elderly, whether it be of normal or of disease state, is thought to produce good results for the elderly.

Further development of nutritional support can improve and maintain the nutritional state of the elderly satisfactorily, and innovative technologies which are mostly based on extracorporeal circulation techniques, can provide not only the method of treatment, but also the method of prevention of the diseases which plague the elderly.

The purpose of this section is to address the advances in the technologies for nutritional support, those being parenteral and enteral feeding; and immunometabolic support.

II. NUTRITIONAL SUPPORT

The method of nutritional support can be divided into two classes, the first being parenteral nutrition, and the other enteral nutrition. In parenteral nutrition, artificially-made nutritional solution is administered intravenously. In enteral nutrition, various nutritious substances are infused into the gastro-intestinal tract. Strategies and details of advances in these technologies are described in the following paragraphs.

A. Marketing strategies

The purpose of applying nutritional support technology is to provide the elderly who are in a malnutritonal state with sufficient nutrients which will support, fully or partially, the life of the elderly well. As a matter of fact, among nursing home residents, 85% of the patients are showing various degrees of protein-caloric malnutrition(3) and 56% of the patients are suffering from severe malnutrition(4). It is thought that the population of the elderly who need nutritional support is quite high.

To further develop reliable technologies for nutritional support would decrease the rate of the malnutritioned elderly and by doing so decrease the number of hospitalized elderly. Also, reducing the number of hospitalized elderly would lessen the need for full medical care which would subsequently lead to cost-effectiveness.

Further developments of technologies for nutritional suppport promise to abolish any complications of devices and warrant the patient being ambulatory without any uncomfortably heavy devices. This would provide the elderly with the chance of a better quality of life.

B. Parental nutrition

The integrated laboratory and clinical investigations which have culminated directly in the development of intravenous hyperalimentation (IVH) started in 1962(5). Thereafter, continuous intense efforts had been made for the completion of total parenteral nutrition (TPN) therapy. The first successful clinical TPN therapy was initiated by Dudrick's group in 1968(6). A 36-year-old woman, with incomplete mechanical small bowel obstruction and ileus secondary to extensive intraperitoneal metastatic ovarian carcinoma, was fed entirely by IVH and was discharged from the hospital to her home. During the last six months of her life, it was possible to maintain her nutrition intravenously at home with a large and heavy hospital apparatus. This apparatus, however, allowed her to be ambulatory and to live with her family. Since this successful clinical application, this technique has become an invaluable tool in the management of certain complicated nutritional problems. With the development of TPN technology, the indications for and the applications of ambulatory home TPN have increased greatly. Indeed, it is estimated that more than 3,000 patients are receiving home TPN currently(7). Furthermore, it is predicted that this number will multiply significantly each year as awareness of the safety and efficacy of home TPN grows, as scientific and technological advances in parenteral feeding techniques and substrates are extended, and as emphasis on cost-effective home health care programs is accentuated(8).

The TPN device consists of five basic components: 1) an implantable catheter for central venous access; 2) bags of nutrient solution which can be prepared by the patient or a family member; 3) an infusion pump to deliver the infusate at a constant rate; 4) a portable stand which serves as an intravenous pole with or without a monitoring device to warn the patient when the infusion is almost completed; and 5) an infusion line with an in-line 0.22-micron filter which moderates transmission of microbes from solution to patient.

Blood access to the patient's central venous system is extremely important for long-term TPN therapy. Due to its hyperosmolarity, TPN requires infusion through a central venous catheter which is usually placed via the subclavian route. The catheter is inserted either by puncture of the subclavian or external jugular vein, or under direct vision by exposure of the cephalic or other similar superficial vein. The catheter tip is advanced until it lies in the superior vena cava at its junction with the right atrium (Fig. 1). The distal end of the catheter is run in a subcutaneous tunnel to emerge through the skin of the chest wall near one of the nipples at a site where the patient can clearly see it. In between infusions the patient fills the catheter with 1.5 ml of heparin solution(1,000 units/ml), a so-called "heparin lock" to prevent clotting within the catheter and to allow mobility(9). As materials for the TPN catheter, polyethylene and silicone rubber (Hickman or Broviac) have been widely used(8,10). It is acknowledged that successful management of the catheter commences with insertion under sterile conditions after meticulous skin preparation. With the use of a standard polyethylene or silicone catheter, however, this procedure has been associated with a 33% incidence of clinically occult subclavian vein thrombosis detectable on a radionuclide venogram(11,12). The requirement for the development of a non-thrombotic catheter lies in the investigation of a more biocompatible material for the catheter. Polyurethane is a promising material and is currently under clinical investigation(12,13). Linden and his colleagues reported that the incidence of clinical thrombophlebitis was less with a polyurethane catheter than with a silicone rubber catheter(12). Also, Fabri and his colleagues reported in their radiographic study that the use of polyurethane catheters in 10 patients showed no evidence of venous thrombosis up to a period of 820 days without the administration of any heparin as an anticoagulant(13). Those studies show that polyurethane is expected to be a suitable material for TPN catheters. Further clinical evaluations by other institutes need to determine its usefulness for TPN. Although care of the catheter is meticulously made, catheter complications with TPN include structural failure, migration, sepsis and thrombosis. To minimize these complications, continuous efforts have been made to develop the implanted vascular access device which consists of a self-sealing silicone rubber septum encased in a port made of metal or plastic attached to a silicone catheter. Currently, several of these devices are under investigation for clinical use (Table II)(14). Fluids, drugs and blood can be administered into this port system by a simple needle puncture through the skin into the port. These systems will minimize the potential for infection and be more cosmetically acceptable to the patient. The need for dressing changes is completely abolished by these systems. Another attempt at trying to avoid indwelling catheter troubles such as thrombosis and infection, has been made by Havil and his colleagues(15). Their basic idea is to create an arterial-venous (A-V) shunt in the arm or leg as a vascular access for the administration of nutrient solutions. Hypertonic solutions fed into such a vein are rapidly diluted and hence relatively nonirritative. By this means a patient can be treated at home without the necessity of hospitalization. For the creation of an A-V fistula, a natural vein graft of a patient or a synthetic graft such as Gore-Tex (W.L.Gore, Inc., USA) is used. This method for home TPN is awaiting further clinical evaluation.

Ingredients of TPN include essential and non-essential amino acids as nitrogen sources, carbohydrates in the form of dextrose and fat as energy sources, various electrolytes, water-soluble and fat-soluble vitamins, essential fatty acids, and trace elements which are especially required in long-term feeding. Typical adult and pediatric home TPN regimens are listed in Table III and Table IV(7). Adjustments in these basic formulations are necessary for each patient depending upon individual requirements, tolerances, body chemistries, and disease process. For home TPN, pre-mixed solutions are supplied by vendors, but solution compounding can be made by a patient himself or by a member of the family without any serious trouble. The self-mix option is among the most difficult of home care techniques, however, no higher risk of infectious complications in mixers has been reported recently(16), not only because of the hypertonic resistance of the solution to microbial growth but also because of the meticulous preparation and adequate sanitary facilities in the home. For the preparation of nutritional formulas for the elderly however, particular considerations must be paid. First, many physiological functions decline progressively throughout adult life. In most cases there is uncertainty about the significance of nutrition in altering the process of these changes. The other issue is that food intake in general diminishes with age, but there is very little solid knowledge on which to base recommendations for the optimum intake of individual nutrients by older people. Because of these reasons, special nutritional formulas for the elderly have not yet been developed. Lack of adequate fundamental data regarding geriatric nutrition has caused emphasis to be placed upon the investigation of the requirements for energy(17,18), protein(19,20) and vitamins(21). Definite data about nutritional requirements for the elderly has not been provided yet. Although there is limited information for the elderly, "recommended dietary allowances" in the USA are available at this time(22).

Realizing that manual flow clamps on gravity-flow systems cannot always maintain the flow rates and the necessity of total volume accuracy required for the infusion of parenteral nutrition solution has led to the development of computerized infusion pumps. Currently, available infusion pumps are listed in Table V. The introduction of infusion pumps has greatly increased the accuracy of the infusion volume intended to infuse in comparison to the conventional gravity-flow system. At this time, however, pumps listed in Table V as general pupose do not satisfy all the aspects of the evaluations(23). These evaluations are made by the following assessments which are: range and accuracy, flow rate continuity, flow rate error change after 24-48 hours operation, accuracy with elevated blood pressures, maximum occlusion pressure, effects of bottle height, operation during transport, drop sensor mispositioning, pump set mispositioning, fluid depletion and air in line, volume counter, keep vein open (KVO) rate. resistance to tampering and accidents, memory functions, alarm disable, battery life, electrical safety, electromagnetic interference (EMI), interference with other equipment, line voltage variation, effects of fluids, quiet operation, ease of use, and servicing(23). Further developments satisfying these aspects are necessary for the success of the infusion pump.

By using these intravenous hyperalimentation technologies, appropriate nutritional conditions can be achieved and maintained for those who are in malnutritional states. These malnutritional states include inflammatory bowel diseases, short-bowel syndrome, certain congenital malabsorption syndromes, pseudo-obstructive syndromes, acute renal failure, acute hepatic failure, the operative malnourished patients, and the complicated post operative or post-trauma patients. Small bowel resection culmunating in short-bowel syndrome is among the most frequent indications for TPN. Necessities such as extended resective procedures arise from bowel infarction, malrotation, gangrenous volvulus, radiation enteritis, unrelenting inflammatory bowel disease such as Crohn's disease and extensive abdominal trauma. Acute flare-ups of inflammatory bowel disease and acute pancreatitis may be treated with periodic TPN therapy, since bowel rest tends to shorten the duration of the acute attack.

Congenital malabsorption syndromes, such as cystic fibrosis and developmental failure of villi, might be a candidate of TPN. Additionally, TPN is indicated in those patients afflicted with various pseudo-obstructive syndromes, such as scleroderma.

Because of the fact that TPN might hasten the ultimate demise of the patient with metastatic cancer disease, full-scale TPN may not be indicated or ethical in the near-terminal cancer patient(16).

These TPN technologies have contributed not only in the improvement of malnutrition caused by inadequate food supply, but also in the therapy of metabolic malnutrition.

One of the serious disorders to plague the elderly is diabetes mellitus. Someone who is suffering from this disease is at a high risk for ischemic heart disease, renal failure, degenerative peripheral neuropathy and retinopathy. Despite intensive efforts with a proper diet, many diabetics need insulin injection therapy to maintain an adequate nutritional state and prevent disastrous vascular disorders. The improvement of insulin therapy can be achieved in many cases when single injections are replaced by continuous insulin infusions. For accurate insulin therapy of a patient, continuous infusion pumps have been developed (Table VI)(24). Further innovation includes an implantable computerized programmable microinfusion pump and a closed loop infusion pump. The implantable open loop insulin pump, which can inject continuously the proper amount of insulin to a diabetic based upon the analysis of blood glucose profiles of a patient, is under clinical investigation(25). This system, however, is not suitable for variations in changeable daily glucose levels of a patient. The closed loop system, which is the glucose-controlled insulin infusion system, is being widely investigated by many laboratories(26,27).

Furthermore, current infusion pump technology could provide the opportunity for the treatment of severe left ventricular dysfunction by strong inotropic agent(28), for controlling chronic severe pain of cancer patients(29), and in treating advanced malignant neoplasma by escalating in doses of chemotherapeutic agents(30,31).

B. Enteral Nutrition

The development of total parenteral nutrition has been a major breakthrough in nutritional technology. In many patients, however, adequate nutritional support can be given with specially formulated liquid diets administered by the enteral route. Enteral nutritional support avoids the potential technical, metabolic, and septic complications of parenteral nutrition. However, it is rather difficult to provide more than 3,000 calories per day by this means.

Patients who benefit from enteral alimentation via a nasogastric feeding tube are those with a normal gastrointestinal tract function who refuse or are not able to take adequate oral alimentation. Those patients include, for example, geriatric, senile dementia and anorexia nervosa patients. In addition, enteral feeding benefits the patients with neurologic or muscular diseases who are unwilling or unable to swallow effectively, such as stroke patients, postoperative neurosurgical patients, and those with multiple sclerosis, myasthenia gravis, and dermatomyositis. Also, patients with obstructing lesions of the proximal gastrointestinal tract may receive benefit from this nutritional support. Those patients include head and neck tumors, esophageal carcinoma, benign esophageal stricture, gastric carcinoma, and gastric outlet obstruction due to chronic duodenal ulcer disease. Such patients usually are fed liquid diets through an enterostomy tube placed distal to the obstructing lesion. In this way, significant malnutrition may be corrected prior to surgical treatment(32).

Enteral feeding tubes are now generally made of silicone rubber or polyurethane(Table VII). Such tubes are expected not to crack or stiffen after prolonged exposure to gastric secretions, a problem that was common with polyvinylchloride. Use of the smallest tube that will allow for passage of the formula is essential to maximize patient comfort and tolerance. The most popular nasoenteric feeding tubes are weighted with elemental mercury or tungsten, which facilitates passage of a small-bore tube into the stomach and when necessary to the duodenum or jejunum through the pyloric sphincter.

When proximal gastrointestinal tract function or continuity is impaired, enterostomy tubes can be surgically placed directly into the stomach or jejunum. Such tubes inserted into the jejunum should be placed as proximally as possible, so that maximal digestion and absorption will minimize the risk of diarrhea(33).

For continuous or scheduled enteral feeding, several enteral pumps are currently available. It is estimated that, at this time, 35,000 enteral pumps have been used at hospitals and nursing homes in the United States for enteral feeding. Such pumps include the Kangaroo pump (Chesebrough-Ponds, Inc.), Dobbhoff pump (Biosearch Medical Products, Inc.), Keofeed pump (IVAC Co.), Rateminder-II pump (Anatros Co.), and Flexiflo-III pump (Ross lab). These electromechanical pumps have recently become available and have been used both for maintaining an accurate infusion rate and in facilitating delivery of the viscous solution through a small-bore tube by application of continuous positive pressure. In addition, usage of such pumps has decreased the likelihood of diarrhea and has permitted more careful assessment of patient tolerance of the enteral formula.

Currently, numerous enteral formulations are available. They differ in osmolarity, digestibility, caloric density, lactose content, viscosity, residue, fat content, taste, and expense. There are several commercially prepared homogenates of selected food items (Table VIII-1.2). When these diets are administered in adequate amounts, these preparations can fully satisfy an individual's caloric and nutritional need. However, a specific nutritional formula for the elderly has not been developed yet.

The major complications of these diets are diarrhea and crampy abdominal pain secondary to the high osmotic load or, occasionally, to an extensively rapid infusion rate.

Further investigations regarding these nutritional technologies include innovating the nutritional formula which can easily be modified to the condition of each individual, and developing the method of assessment of the effectiveness of nutritional support for the individual nutritional state.

III. THERAPEUTIC APHERESIS

As mentioned before, nutritional states of the elderly are greatly related to the malfunction of the immuno-metabolic system, which is common in geriatric people. So, it is considered important to correct the abnormalities of metabolism which increase with aging. In this aspect, therapeutic apheresis, especially on-line plasma treatment with returning essential nutrients, is an approach to preserving nutritional and immunological homeostasis.

Therapeutic apheresis is the use of a procedure to separate components of the blood followed by removal of one or more of these components. This procedure is used therapeutically to remove cells or solutes which are thought to be harmful(34). The idea of therapeutic apheresis is over 3,000 years old. People who were performing the role of medical doctors today had been cleansing the body of sick patients by blood letting to get rid of the foul and noxious matters(35). Recent successes of extracorporeal technique, blood access, membrane technology and centrifugal technology have turned this old dream into the reality of a scientific realization.

Blood is divided into two components which are plasma and cell components. In cell components, three basic cell types exist: red blood cells, white blood cells and platelets. There are several modalities which deal with the subject of plasma or of some solutes in plasma. In such modalities, there are therapeutical plasmapheresis (plasma exchange), thermofiltration and cryofiltration. Cytapheresis is intended to remove certain cell components from the whole blood.

Details of these modalities are to be described in the following paragraphs.

IV. METHODS OF PLASMA SEPARATION

For the separation of the plasma in the blood, there are two basic approaches. One is membrane plasma separation and the other is centrifugal plasma separation (Fig. 2)(36).

The principle of plasma separation by membrane separators is to separate the noncellular components of the blood from the cellular components of the blood by using porous membranes (Fig. 3). Several materials for the porous membrane have been developed for clinical use (Table IX), those being cellulose diacetate (Asahi Medical Co., Teijin Co., Terumo Co., Japan), polyvinyl alcohol (Kuraray Industrial Co., Japan), polymethylmethacrylate (PMMA) (Toray Industries, Inc., Japan), polyethylene (Mitsubishi Rayon Co., Japan), polypropylene (Fresenius Co., West Germany, Takeda Medical, Japan, Travenol Co., USA), polyvinyl chloride (Cobe Co., USA). These membranes are made with a porosity ranging from 0.2 - 0.6 um (Fig. 4).

There are two types of housing for these membranes, with one being a hollow fiber type (Fig. 5) and the other being a plate type (Fig. 6). As a membrane plasma separator, the hollow fiber type is very common. The outlook of the hollow fiber type is very similar to the hemodialyzer; however, operation of a membrane plasma separator is quite different. Dialyzers for hemodialysis and hemofilters for hemofiltration require high transmembrane pressure, while for sufficient operation of a membrane plasma separator, particular considerations must be paid, those being: a) high plasma separation rates with high sieving are possible at low transmembrane pressure, generally below 50mmHg(37); b) increasing transmembrane pressure leads to deterioration of plasma flux, sieving and hemolysis(38); c) the nature of the blood and its cellular and macromolecular concentrations will greatly dictate operation limits(39) (Fig.7). Generally, plasma is separated easily at a rate of 30ml/min with a blood flow of 100ml/min.

For the centrifugal separation, several varieties of centrifugal apparatus are available, including intermittent flow and continuous flow instruments (Table X). The process of the intermittent separation is drawing the blood by pump, separating the blood into components by centrifugation and then reinfusing cellular components, discarding, or treating the plasma. In continuous separation, these processes are performed successively. Centrifugal machines have been made by three manufacturers; IBM (USA) and Fenwell (USA) are making continuous centrifugal apparatus and Hemonetics (USA) is making intermittent centrifugal machines.

By centrifugal separation, plasma is separated at 15-25ml/min with the blood flow being 40-60ml/min. Disadvantages of this procedure are: a) plasma may not be separated completely from the cellular components of the blood and platelets can be removed in the plasma(40); b) the apparatus is so big and heavy that the transportation is not very easy.

Separated plasma includes all kinds of soluble substances in the blood, which are albumin, globulin, immune complexes, electrolyte and so on. Pathological macromolecules which are distinct in some diseases are the subject of plasma treatment, but in diseases where pathological macromolecules are not determined, plasma exchange has a potential modality for clinical therapy.

V. THERAPEUTIC PLASMAPHERESIS (Plasma Exchange)

Plasma exchange is a method by discarding separated plasma to remove pathologic macromolecules which are not excluded by conventional hemodialysis and hemofiltration. By using this technology, many diseases which are considered difficult to treat by conventional therapy have become possible to be treated effectively. These diseases include rheumatilogic, hematologic, neurologic, and other immuno-metabolic disorders (Table XI).

All of these diseases however, which have been treated by plasmapheresis, are not always the object of plasmapheresis. This is because this method has limitations, such as (a) the requirement of plasma products (albumin solution, fresh frozen plasma, plasma protein fraction), (b) loss of essential plasma solutes creating possible immunologic and nutritional deficiencies and (c) potential contamination by plasma substitutes(41).

In spite of these limitations, the use in numbers of plasmapheresis is increasing year by year(42). With the increase in the number of plasmapheresis procedures, the quantity of plasma products which are purchased for this therapy has been increasing remarkably. This increase in the demand of plasma products is envoking a big ripple, to the blood business, which in turn, is falling into a chronic shortage of blood donations(43). Recently, however a technology for the selective removal of pathogenic macromolecules has been developed and is under clinical investigation. None or little plasma products are required by this technology, which would therefore reduce the tendency of an increase in the demand for plasma products.

Further, on-line plasma treatment by its selective separation of the pathological macromolecules eliminates the need for supplements that would normally be lost by plasma exchange. Such technologies prevent further nutritient depletion in such patients who may already have a compromised nutritional status.

In the case of acute hepatic liver failure, however, the pathogenic substances responsible have not been clearly determined yet, and the prognosis by conventional therapy is extremely poor. Plasmapheresis is thus a good modality of treatment at this moment. As a matter of fact, the recent positive prognosis for acute liver failure with the use of fresh frozen plasma has been increasing from 15% by conventional therapy to 35% by plasmapheresis therapy(44).. Thus, plasma exchange may have a high probability for effective therapeutic treatment of metabolic disorders, but this method must be considered for proper application and practice.

VI. PLASMA TREATMENT

Plasma treatment is the method intended to remove pathological molecules selectively. By this method, loss of essential plasma, the requirement of plasma products which are observed in plasmapheresis, can be reduced effectively. On-line plasmapheresis provides a suitable methodology for this plasma treatment. Plasma separated by a membrane separator is processed for cryofiltration, thermofiltration, cascade membrane filtration (Fig. 3) or sorbent treatment. Treated plasma is then returned to the patient with its cellular components (Fig. 9)(45). These current technologies are reviewed briefly.

A. Cascade Membrane Filtration

Once plasma is separated from the cellular components, it is easy to remove certain toxic substances, as well as to add to this system. If we know certain macromolecules should be removed, we can use cascade membrane technology(46) to selectively remove molecules of a few million daltons molecular weight (e.g., immune complexes), or below 100,000 daltons molecular weight (e.g., albumin fractions) (Fig. 10)(47). For this purpose, several secondary filters have been developed by several industries (Table XII). Clinical application of this procedure is under investigation, however, autoimmune diseases such as systemic lupus erythematosus and thromboangitis obliterans, which are difficult to treat by conventional therapy, have shown remarkable improvements by this method. Also, it has been possible to treat arteriosclerotic obliterans which is common in old age and in which in its progressive stage, amputation of the leg is often its final treatment(48).

Thus, this technology is promissing as a therapeutic modality in clinical application, but further effort to develop filters which have a property corresponding to molecular abnormalities of various immuno-metabolic diseases must be performed continuously.

B. Cryofiltration

Cryofiltration is a form of plasma therapy that consists of the on-line plasma cooling and filtration of plasma for the removal of macromolecular plasma solutes from patients with immune-mediated diseases (Fig. 9 middle).

Immune complexes are formed in the body of autoimmune diseases and are found in the circulation. They are pathologic molecules with molecular weights of greater than 100,000 daltons, but because of the physiochemical properties of the molecules and the membrane properties, it is difficult to use a simple membrane filtration system effectively to separate those macromolecules from albumin or small molecules. From the finding that white turbid cryoprotein is very often present in refrigerated plasma which was taken by plasmapheresis from the autoimmune disease state, an attempt was made to utilize the phenomenon of cold separation to accelerate the effective separation of albumin and cryoproteins. Cryofiltration was developed by Malchesky and Nose' in 1980(47,49). This process involves rapid cooling of the plasma in an on-line system to form cryogel, which is then filtrated under cold conditions. The cryogel is retained on the filter and lower molecular weight solutes are returned to the patients. This cryogel contains a number of substances found in plasma, such as immune complexes, Rheumatoid factor, immunoglobulins and fibrinogen (Table XIII)(50,51). This system has been used to treat several immune mediated diseases including rheumatoid arthritis, rheumatoid vasculitis, systemic lupus erythematosus, cryoglobulinemia and cold-agglutinin hemolytic anemia. The patients over 60 years old who did not respond to conventional therapies showed 80% good or excellent responses(52). Remarkable decreases in immune complexes and immunoglobulins by cryofiltration are noted in rheumatoid arthritis patients, with clinical improvements such as Ritchie index, grip strength, 50 feet walking time and duration of morning stiffness(50,53).

Cryogel, which is removed with cryofiltration, is formed continuously from heparinized plasma in relatively short time (10-20 minutes) at near freezing temperatures(54,55). Cryoprecipitate is similar to cryogel but several distinctions can be made between them, because cryoprecipitate is formed from serum during three to five days at 4°C environmental temperature. From the observation that cryogel contains many immune related substances and that reduction of cryogel accompanies the clinical improvements, cryofiltration possesses great possibilites in the treatment of a variety of autoimmune mediated diseases(45).

C. Thermofiltration

In cryofiltration, the regulation of the plasma temperature has a certain effect on the selection of macromolecules which aggregate in the cold. An in vitro attempt to study selective removal of several solutes in plasma at varying temperatures up to 37°C, was made in 1983(55). By using Kuraray EVAL 4A filter (Kuraray Industrial Co. Japan), successful in vitro separation of high density lipoproteins (HDL) from low density lipoproteins (LDL) was noted at a physiological temperature(56,57). LDL cholesterol levels have been shown to have a high correlation with the risk of coronary heart disease, while HDL cholesterol shows a strong inverse correlation(60). The idea of thermofiltration, which is the plasma treatment procedure with plasma filtration at near or above normal physiologic temperature, was contrived and named by Nose' in 1984(59). The first clinical application of this method was made in 1985 for a 39 year old patient that had sclerosing cholangitis, with a high concentration of cholesterol (210-450mg/dl) and a very high LDL/HDL cholesterol ratio (8.61)(60). The patient tolerated this procedure well. Results showed that the LDL/HDL cholesterol ratio decreased to 6.96, with the reduction of the LDL-VLDL cholesterol level by 33.3%. In the performance of thermofiltration, plasma substitute is not required. From these observations, by using this technology it has become possible to reduce abnormal plasma LDL cholesterol levels. In addition, this methodology has great possibilities, not only in treating the end stage of artheriosclerosis, but also in preventing the disease in the elderly. This technology can also be applied to other diseases which contain within the patient's plasma, some cellular toxic or inhibitory factors which can be destroyed by heat exposure, as in cancer or hepatic failure patients(61).

D. Sorbent Treatment

Since 1963, metabolic assist systems for the support of hepatic failure patients have been developed in conjunction with membrane plasma separation. Noble initial trials, however, did not result in good responses, because of the immature technology of plasma separation at that time(62). Meanwhile, numerous techniques have been used for solute removal for hepatic support, including hemodialysis(63), hemofiltration(64,65), direct hemoperfusion of activated charcoal(66) and plasmapheresis(67). Both hemodialysis and hemofiltration, however, have had limits in their applications for hepatic assist, because of the nature and size of metabolic substances occurring in hepatic failure. Direct hemoperfusion with activated charcoal and various resins also have had limits, because of their biocompatibilities. Plasma treatment with metabolic and/or detoxification systems is the only method to solve the problems mentioned above.

The methods of on-line plasma treatment with fresh sliced liver tissues and with multi-sorbents, was devised by Nose' and his colleagues in 1974(68), and 1978(69). Further, an attempt with cultured hepatocytes which would realize both of the metabolic and detoxificative functions of liver, is under experimental investigation. Multi-sorbent systems contain anion exchange resin and activated charcoal for the removal of middle and macromolecules. Average reduction of bilirubin which increases in hepatic failure, is approximately 31% per treatment. Initial trials for acute liver failure did not show remarkable responses(70), but cholestatic patients with symptoms of pururitis, xanthomatous skin lesions and jaundice, showed dramatic improvement and surprisingly, a long alleviation of these symptoms(71). These experiences indicate that membrane plasmapheresis with on-line detoxification can be used effectively on a chronic basis for hepatic support.

Because of nonspecific sorption characteristics of the sorbents, their use was limited clinically. Recent works, however, for developing immunosorbents, which are specific for the removal of the immunoproteins that subsequently increase in autoimmune disorders, are of expected value for the selective removal of macromolecules (Table XIV)(72). In these systems, biological materials are immobilized in solid adsorbents, which are then utilized in the form of plasma treatment or direct hemoperfusion. While this technology is a promising one for immuno-assest, it is necessary to hurry determining the entity of the diseases with unknown immuno-metabolic disorders.

Currently, this technology is under investigation not only for autoimmune diseases, but also for cancer(73).

VII. CONCLUSION

Current progress in nutritional support technologies has made possible the treatment of chronic malnutritional patients at home.

Also, current progress in immunological-metabolic assist technologies especially plasma separation and plasma treatment technologies, has opened the way for the treatment of immuno-metabolic diseases which are considered to be difficult to treat by conventional therapies. By using current available technologies, it has become possible not only in treating the disease state, but also in preventing the immuno-metabolic disorders which are common in the elderly. Further development and innovation of nutritional technologies will promise the satisfactory improvement of the malnutritional state of the elderly. By supporting adequate nourishment which is adjusted to each individual patient and correcting these disorders using progressed methodologies, the improvement of the nutritional state in the elderly can be achieved. In order to sustain or provide a better quality life for the elderly, current artificial organs technologies can play an important role.

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TABLE I

Normal fibrinogen values in humans

Age (yr)	Value (mg/dl)
10–19	185–300
20–29	185–340
30–39	177–365
40–44	215–400
50–59	235–455
Over 60	260–500

TASK V: ADVANCES IN ANTIBIOTICS

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TASK V: ADVANCES IN ANTIBIOTICS

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I. OVERVIEW

In order to cope with the various types of infections, many types of antibiotics are clinically available. On the other hand, new drugs which deal with infections typical to senior citizens have been enthusiastically investigated. These include beta-lactam antibiotics, liposomal Amphotericin B and quinolones. High molecular compound drugs, with improved efficiency continuity and stability with less toxicity, and interferon have great potential application for the infection problems in the aging population.

In addition, direct continuous intravenous delivery of anti-infectious agents in a safe and accurate manner, is one of the most important key technologies in order to produce the maximum effects of these drugs. Simple, accurate drug delivery infusion pumps are available in at least 30 different designs. They are currently very widely used, not only in the hospital but also in the home environment. Utilization of drug delivery infusion pumps at home has contributed to the cost containment program of the patient who suffers from recurrent, persistent infections. Recent developments in new drug delivery systems have advanced quite remarkably. Liposome microcapsule, polymeric drug delivery systems, osmotic pumps and implantable infusion pumps are becoming more and more realistic.

In the elderly population, the resistance against infection and the susceptibility to various types of infections are the major medical concerns. This is due to the altered host defense mechanisms in the elderly. Even though some understanding of this phenomenon are available, more clarification is still mandatory in order to cope with this most difficult medical problem. This infection prone situation might be referred to as one of an age-induced immunodeficiency syndrome. Through several personal communications, we recently learned that a Russian scientist, Dr. Nikolaiev in Kiev, demonstrated possible life extension of aged mice by feeding them activated carbon. He also suggested that similar effects are expected by the use of direct hemoperfusion of activated carbon in aged experimental animals. Although scientific documentation is not available, this experience suggests the involvement of humoral factors in the aging process.

Some form of treatment of infection in the elderly should be considered for these age induced humoral and cellular abnormalities. Simple antibiotic treatment is not expected to be as effective as the same treatment regimen for the younger generation. Efforts to normalize these age induced immunological abnormalities should be combined with antibiotic therapies. Therefore, in order to cope with infectious diseases in the elderly, not only development of new antibiotics and new drug delivery systems, but also development of immunomodulation technologies should be enthusiastically pushed on.

II. PRESENT STATUS AND FUTURE POSSIBILITIES

1. Altered Host Defense Mechanisms in the Elderly

The decreased resistance to infection in the elderly is a problem of long-standing interest. Recently, with aging of their populations, a renaissance of concern with this problem has occurred in industrialized societies.

Resistance to infection in the aged is altered. A number of factors complicate the understanding of the cause of this alteration. However, the available information supports the hypothesis that T-cell function is altered in the aged. Peripheral blood lymphocytes from elderly volunteers in 3-day culture synthesize DNA less actively upon exposure to nonspecific mitogens or allogenic lymphocytes than do lymphocytes harvested from younger controls(1,2). The duration of the cell cycle is prolonged, perhaps accounting for the increased time required to reach peak response(3). Potentially, some type of thymic factor therapy could correct these abnormalities.

Chemotactic responses are normal in the majority of aged individuals studied(4). In contrast, when hospitalized patients were studied, the prevalence of polymorphonuclear leukocyte dysfunction was increased in all age groups(5). Recently, Charpentier and colleagues noted an alteration in oxidative metabolism of polymorphonuclear leukocytes and depressed phagocytosis, as evaluated by microscopy, in aged patients(6). There are some humoral factors that can enhance or in certain disease states inhibit the polymorphonuclear leukocyte ability to respond to infection. Such humoral factors include specific antibodies, and antiglobulins which in vitro can inhibit phagocytosis, complement, and various inhibitors of chemotaxis described in individuals with neoplastic and hepatic disease(7,8). These studies indicate that the function of polymorphonuclear leukocytes or lymphocytes in elderly people under no stress may differ considerably from that observed when they have developed a moderate or severe illness(9).

2. Development of New Drugs

(a) The Newer Antibiotics

Various kinds of cephalosporins have been released since the discovery of a fungus, Cephalosporium acremonium[10] (Fig. 1).

The term "generations" is used as a tool to describe the gram-negative enteric bacillary activity of the cephalosporins. Although, currently available third-generation cephalosporins, which include cefotaxim (Haechst-Roussel), ceftizoxime (Smith, Kline & French), cefoperazone (Pfizer), ceftriaxone (Roche), and cefsulodin (Abbott) are marketed as antipseudomonal drugs, they fail to provide adequate activity against many Pseudomonas aeruginosa, one of enteric gram-negative bacilli. At present, three investigational beta-lactam antibiotics are much more potent for P. aeruginosa: ceftazidime (Glaxo), aztreonamm (Squibb) and imipenem (Merck)(11).

Much attention has been given to the synthesis of quinolones and to the evaluation of these newly prepared agents for antibacterial activity. The fluoroquinolones are very potent synthetic agents active against the enteric gram-negative bacilli and cocci, including P. aeruginosa(12).

Pneumonia and influenza together constitute the leading infectious cause of death in the elderly and the fourth most common cause of death overall in the elderly (Table I). Newer drugs described above are promised to be useful in treatment of these infectious diseases in the elderly.

Although the classical method of developing new drugs including the discovery of new agents and the modification of their structures needs tremendous efforts, a large number of newer antibiotics will be continuously introduced for clinical use in the United States.

(b) Designs for Development of High Molecular Compound Drugs

In generally speaking, high molecular compound drugs are so-called polymeric forms of drugs. Low molecular units of these polymers are effective as known drugs. Polymeric forms are designed for improvement of efficiency continuity, for better stability, for less toxicity, for slow release of active units, and so on.

Ringsdorf reported the basic structural design of high molecular compounds as drug-carriers(13). On its main polymer chain, the basic structure should contain three functional units:

1) Soluble Unit

This unit is a non-toxic co-polymerized block which is soluble in water and lipid.

2) Drug Unit

The specified bonding for fixation and release of the lower molecular drug should exist in this unit.

3) Transfer Unit

The function of this unit is specified attachment of the drug onto the target site. Available characteristics for the function are interactions of receptors, pH dependency, molecular weights and structures, and so on.

So far, studies on synthetic high molecular compounds for utilization as drug carriers have not succeeded. Recently, native polymers have attracted the attention of researchers(14). Since native polymers are generally superior in biocompatibility and non-toxicity, some of those compounds, e.g. soluble starch, might be available for carriers in high molecular compound drugs.

Not only Ringsdorf's concept, Goldberg also reported the concept of polymeric affinity drug design(15).

Investigations in this field should be enthusiastically pushed on for development of new drugs to specifically treat diseases of the elderly patient.

3. Development of New Drug Delivery Systems

(a) The Liposome as a Microcapsule

The liposome is a neutral or acidic lipid vessicle which can hold drugs within its membrane of two lipid molecule layers. The membrane acts as a barrier against water soluble substances such as ions and high molecular non-ions. Expected functions of liposome-capsule drugs are as follows:

1) slow release of drugs

-----long acting efficiency

-----inhibition of toxicity and anaphylaxis which may be encountered when drugs are given in large doses.

2) improvement in capability to approach target sites

3) bacteriocidal effect on intracellular and intra-lysosomal bacteria

Trials to achieve above mentioned results have already succeeded to a certain extent. Some agents were improved in those permeability through the blood-brain barrier with liposome microcapsules(16). One of the valuable preparations is liposomal Amphotericine B which reduces the toxicity and enhances the efficacy of its free form against fungal infections(17) (Fig 2).

Since the effectiveness of free form Amphotericine B (Squibb) which has been the drug of choice for most serious systemic fungal infections is limited due to the severity of its acute and chronic toxicity, liposomal Amphotericine B is highly beneficial in the treatment of fungal infections in the elderly. Although undesired side effects of liposome microcapsules have been noted in humans(18), no evidence of chronic toxicity was observed in long term patients treated with liposomal Amphotericine B(17). Successful results have also been reported regarding B(19,20). Not only utilization of antigen-antibody reactions, receptor specific reactions and physicochemical phenomena such as temperature effect have been investigated(20); however, more enthusiastic effort is required to obtain target cell specific characteristics of liposomes.

(b) Polymeric Drug Delivery Systems

Biodegradable drug delivery systems have been developed using native high molecular compounds such as geratins. These systems implanted under the skin offer potential advantages in both release rate controlability and biodegradability. They achieve relatively constant release rates for about three days. Other polymer matrix drug delivery systems have been developed which permitted sustained release of high molecular drugs. Ethylene-vinyl acetate copolymers are common materials for matrix substrates. A variety of shapes of systems to achieve constant release rates were analyzed from a theoretical standpoint(21); the best results were with a hemispheric device laminated with an impermeable coating, except for a small concavity in the center face (Fig. 3). This can be envisioned as a small cantaloupe cut in half, where the orange pulp of the melon is the drug. The melon half is then coated everywhere except where the seeds were, so all the drug must be released through the small exposed section. Systems with these geometries do achieve constant release rate for macromolecular agents for over 60 days(22). Not only as antibiotics delivery systems for chronic infections, these systems are also expected to be used as interferon delivery systems.

(C) Osmotic Pumps

Recently, membrane-controlled osmosis has been used as a basis to achieve rate-controlled drug release. Two types of osmotic pump systems have been reported: an oral dosage form(23), and an implantable form(24). Each system contains a core of solid or liquid drug, coated with a semipermeable membrane having a single small orifice. The membrane selectivity admits water from the outside, which enters because of the osmotic activity of "osmotic core". The membrane structure does not allow expansion of the system volume; thus, fluid containing the drug must leave the interior of the system at the same rate that water enters by osmosis. An oral dosage form (Oros (TM)) probably working effectively as a one a day dosage form of antibiotics (Fig. 4). The implantable osmotic pump system (e.g. Alzet (TM)) achieved constant release rate (1 microliter/hr) of agents for over 1 week(24), and expected to be useful for antibiotics delivery system because of its high rate controlability.

(d) Implantable Infusion Pumps

One of the implantable infusion pumps which has been developed and tested is named Infusaid (Infusaid Corp., Sharon, MA). It is a disc-shaped cannister of light weight, biocompatible titanium, which contains a collapsible welded bellows. The bellows separates the cannister interior into two chambers, one of which contains a vapor-liquid mixture of a fluorocarbon propellant, the other containing the infusate. At body temperature, the vapor pressure exerted by the chemical power source forces fluid from the infusate chamber, and provides a constant rate of fluid ejection at a given temperature (Fig. 5). A large pump of this type has several advantages over the polymeric delivery systems, including:

1. the ability to deliver large volumes of fluid
2. versatility of drug administration
3. the nonthrombogenic delivery cannula allows a drug to be delivered into specific blood vessels or body cavities
4. the pump can be recharged without the need for reimplantation procedures

The pump is now undergoing clinical trials for infusion of anticoagulants(25), anticancer agents(26), insulin(27) and so on. Implantable infusion pumps have a possibility to be useful for the the treatment of chronic infections.

4. Immunomodulation

Since the occurrence of infectious diseases in the elderly is based upon the age-induced immunodeficiency state, it is significantly beneficial to correct and to control the altered difference system. This process is called "Immunomodulation". At present, the development of immunomodulation technologies is one of highly innovative fields in medical sciences.

(a) Immunoactive Cell Infusion

Fresh leukocytes infusion is a useful and relatively common method for the treatment of uncontrollable infectious diseases accompanied by agranulocytosis. A large amount of fresh leukocytes can be harvested from a donor with plasmapheresis technologies. Not only leukocytes infusion, lymphocytes infusion may be useful in immunosuppressive elderly patients. Herzenberg has reported the method to sort T-cells and B-cells from donor blood(28). Other sophisticated sorting technologies have been reported also(29,30).

(b) Immunoactivation

1. Polymer-Blood Interaction

As far as blood compatibility is concerned, the smaller the interaction between a polymer and blood is, the better the polymer is for blood contacting material. The effort to develop better biomaterials have been directed to diminish the material blood interaction.

On the other hand, Cellulose membrane-blood component interactions, transient leukopenia and complement system activation have been noted since 1960(31). Recently, the immunomodulating effect of biomaterials through polymer-blood interactions have been enthusiastically investigated. These include increments of phagocytosis by polymer membranes(32), lymphocyte activation by immobilized hemaglutinin(33), complements activation by Sepharose-serum protein A(34), and Sepharose alone(35). This immunoactivating effect has been used already for the treatment of cancer(36).

It is highly suggestive that a large number of polymeric membrane can modulate immune systems in different manners. Although various kinds of interactions between polymeric membranes and immune systems require further studies, this method might be possible to apply for treatment of infections in the elderly immunosuppressed.

2. Interferon Inducer

Interferon was discovered as an antiviral protein by Isaacs and Lindenmann in 1957(37). In addition to its antiviral effect, interferon has been found to suppress tumor growth and modulate the immune response. Its chemical structure has not been precisely identified yet, however, interferon may become a major part of therapy for viral diseases including chronic active hepatitis due to hepatitis B virus, herpes virus-induced infections, cytomegalovirus infections, and acquired immunodeficiency syndrome(AIDS). It also holds promise for the treatment of certain cancers(38).

The clinical use of interferon is presently limited, to a certain degree, by its many side effects including fever, fatigue, proteinuria, increased transaminases, and so on.

Since all side effects appear to be reversible and most are dose dependent, interferon therapy may have particular value for patients who are immunosuppressed.

Not only production of interferon by DNA recombinant methods (genetic engineering)(39), induction of interferon by high molecular compounds has attracted a large number of investigator's attention. Interferons are now classified into three types: alpha, beta and gamma interferons. Beta interferon can be stimulated in tissue culture with synthetic polyribonucleotides. The polyinosinicpolycytidilic acid has been known as the most active inducer of the beta interferon(40). The maleic acid co-polymer, the polyacrylic acid, the divinylether-maleic acid co-polymer and other poly-saccharides have been extensively investigated as beta interferon inducers(41). Interactions between cells and polymeric agents which have the activity to induce the beta interferon requires further study but shows promise for the treatment of viral diseases and some cancers.

3. Other Immunomodulating Agents

With the discovery of new and pharmacollogically better described agent, the pursuit of a method for the enchancement of nonspecific host defense against bacterial infection has received a new infusion of interest(42-47). Muramyl dipeptide is a nonspecific immunostimulant defined as the smallest fragment of the mycobacterial cell wall capable of adjuvant activity(43). Some investigators have reported that the agent is effective against many different bacterial challenges(44-46). So far, Muramyl dipeptide has not seemed to have a beneficial effect when given after the time of injury but before the time of bacterial challenge. However, because of the apparent safety and efficacy inferent in the use of the agent, clinical trials seem warranted.

Liposomes are known as potential immunomodulators which induce antibodies, activate immune systems, and macrophages, and so on(47,48). Although further investigation is necessary, it can be useful for infectious diseases in elderly patients whose defense systems are suppressed.

(c) Immunoadsorption

In order to remove abnormal immunocomplex from patients of various kinds of immune diseases, plasmapheresis technique has been extensively used(49) (Fig. 6). Recently, using this technique, immunoadsorbent therapies for infectious diseases have been investigated.

These include endotoxin adsorption by immobilized Polymixin B(50), phagocytable substance removal using the charcoal filter in sepsis(51), and hepatitis B antigen adsorption using immobilized antibody filter(52). The charcoal filter application to septic patients have already succeeded to a certain extent(51). The immunoadsorption described above can be useful as a supportive method for the treatment of infectious diseases.

The normalization of the humoral factor abnormalities induced by the aging process can be achieved by new immunomodulation technologies. It is highly anticipated that normalization of age induced immunological abnormality will enhance the effects of anti-infectious treatments available for the elderly.

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LEGEND OF TABLES

Table 1   Death rates by sex, age, and selected causes: 1980

DEATH RATES BY SEX, AGE, AND SELECTED CAUSES: 1980

(Deaths per 100,000 resident population enumerated as of April 1. Causes of death classified according to ninth revision of the *International Classification of Diseases*)

CAUSE OF DEATH	Total [1]	MALE					FEMALE				
		Total [1]	15–24 years	25–44 years	45–64 years	65 yrs. and over	Total [1]	15–24 years	25–44 years	45–64 years	65 yrs. and over
All causes [2]	878.3	976.9	172.3	238.0	1,270.0	6,387.9	785.3	57.5	110.2	573.9	4,484
Diseases of heart	336.0	368.6	3.7	24.5	505.3	2,778.6	305.1	2.1	11.9	177.3	2,227.6
Malignant neoplasms	183.9	205.3	7.9	25.3	348.0	1,271.5	163.6	4.3	32.1	265.9	[illegible]
Cerebrovascular diseases	75.1	63.6	[illegible]	5.1	50.0	557.0	85.1	.3	[illegible]	[illegible]	[illegible]
Accidents and adverse effects	46.7	57.4	96.7	58.6	51.3	124.4	27.1	25.0	[illegible]	21.6	[illegible]
Chronic obstructive pulmonary diseases [3]	24.7	35.1	.4	1.0	35.0	297.3	15.2	.2	.9	17.6	[illegible]
Pneumonia and influenza	24.1	25.1	.8	2.3	17.8	212.5	23.2	[illegible]	.8	[illegible]	[illegible]
Diabetes mellitus	15.4	13.3	.3	2.7	19.2	92.8	17.6	.3	[illegible]	[illegible]	[illegible]
Chronic liver disease and cirrhosis	13.5	18.0	.3	10.3	50.5	56.0	9.3	.3	5.0	23.2	24.8
Atherosclerosis	13.0	10.5	-	.1	4.0	104.0	15.3	-	.1	2.0	[illegible]
Suicide	11.9	18.6	20.2	24.0	23.7	35.0	5.5	4.3	7.7	8.9	6.1
Certain conditions originating in the perinatal period	10.1	11.9	(X)	(X)	(X)	(X)	8.4	(X)	(X)	(X)	(X)
Homicide and legal intervention	10.7	17.3	24.5	29.4	15.4	9.9	4.5	6.6	6.4	3.4	3.3
Nephritis, nephrotic syndrome and nephrosis	7.4	7.8	.2	1.2	7.1	53.6	7.0	(Z)	.7	5.5	42.1

- Represents zero. X Not applicable. Z Less than .05.

[1] Includes persons under 15 years old, not shown separately.

[2] Includes other causes, not shown separately.

[3] Includes allied conditions.

Source: U.S. National Center for Health Statistics, *Vital Statistics of the United States*, annual, and unpublished data.

[illegible]

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LEGEND OF FIGURES

Figure 1 Cephalosporins marketed in the U.S.

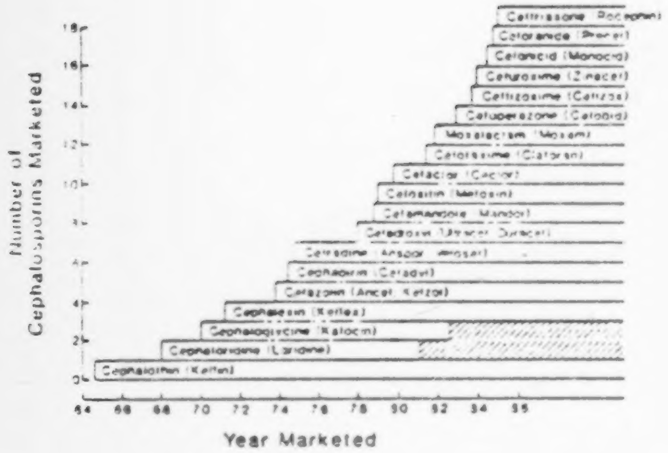
Figure 2 Effect and toxicity of free versus liposome-encapsulated amphotericin B

Fibure 3 Schematic diagram of zero-order release system for macromolecules

Figure 4 Schematic diagram of Oros$^{\text{TM}}$ system

Figure 5 Top view of Infusaid$^{\text{TM}}$ implantable infusion pump

Figure 6 General scheme of plasmapheresis



Cephalosporins marketed in the U.S.

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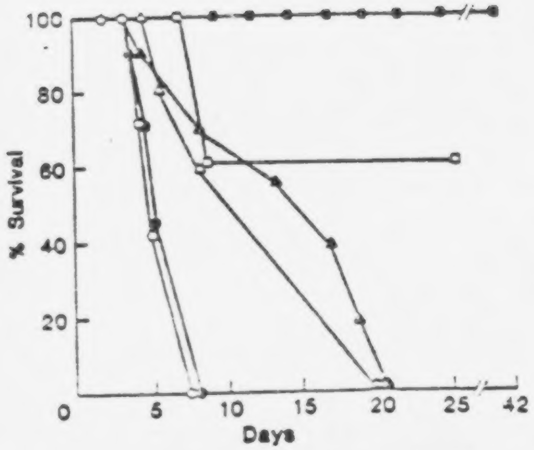
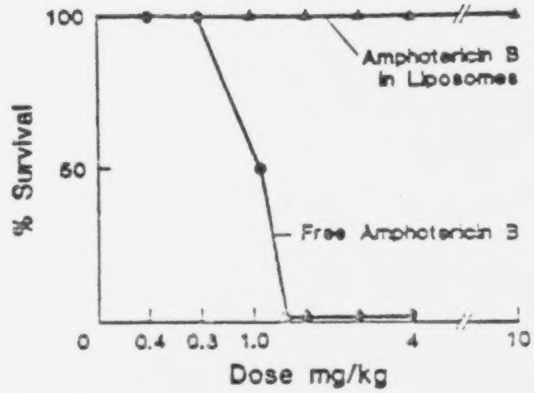


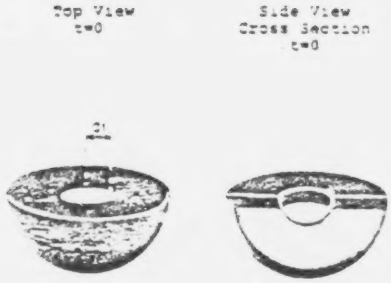
Effect of liposome-encapsulated amphotericin B on survival of mice infected with *Candida albicans*. Two days after iv administration of *C. albicans* the animals were either (●) not treated (controls) or treated with (○) empty liposomes (400 mg of total lipid/kg); (▲) free amphotericin B (0.8 mg/kg); or liposome-encapsulated amphotericin B in doses of (△) 0.8 mg, (□) 2 mg, or (■) 4 mg of amphotericin B in 400 mg of total lipid/kg.



Toxicity of free versus liposome-encapsulated amphotericin B in mice. The total lipid dose was 400 mg/kg.

[illegible]

(From: Lopez-Berestein G et al: Treatment and prophylaxis of disseminated infection due to candida albicans in mice with liposome-encapsulated Amphotericin B. J.Infec.Disease 147:939,1983)

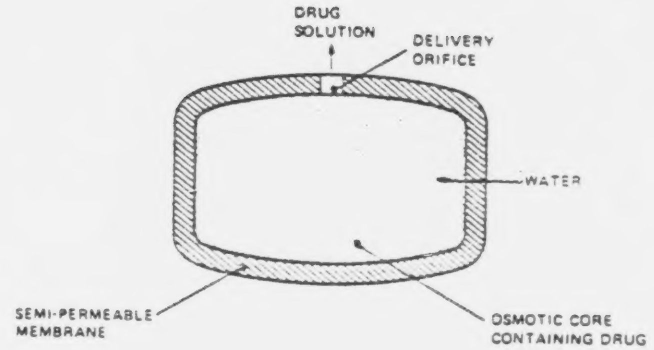


Schematic diagram of zero-order release system for macromolecules.

Fig.3

(From Langer R et al: Implantable [illegible] delivery systems.

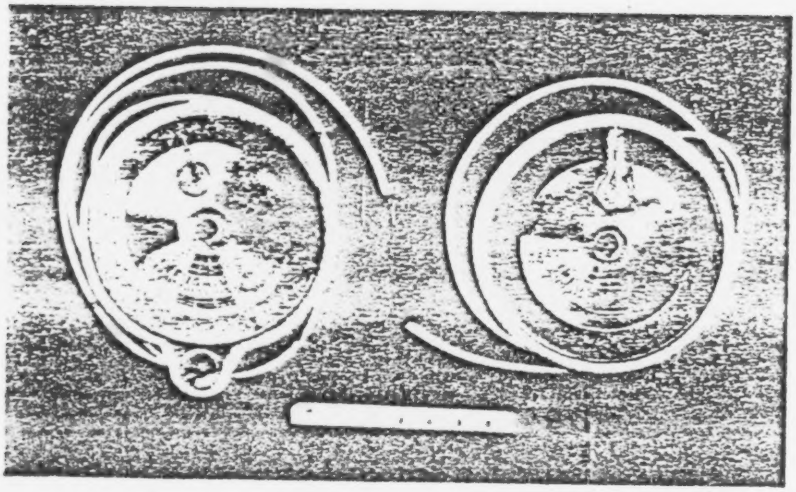
Trans.Am.Soc.Artif.Organs 27:5[illegible]



Schematic diagram of Oros® system.

Fig.6

([illegible] Langer R et al: Implantable drug delivery systems.
Trans.Am.Soc.Artif.Organs 27:[illegible],[illegible])



Top view of Infusaid™ implantable infusion pump.

Fig.[illegible]

(From: [illegible] et al: Implantable [illegible] [illegible] [illegible].

Trans.Am.Soc.Artif.Organs 27:[illegible],[illegible]

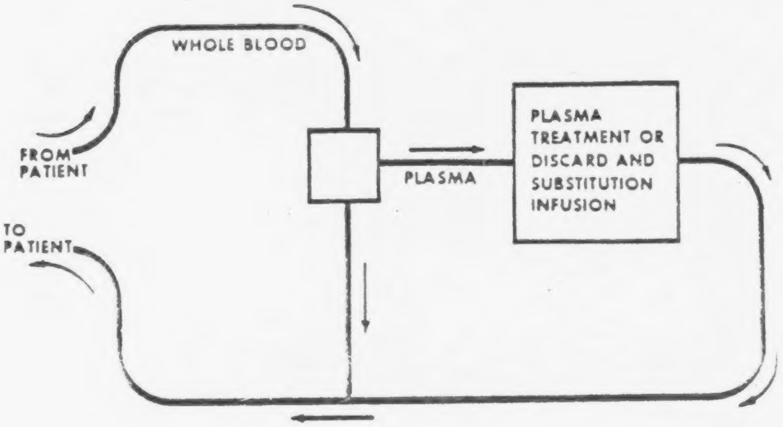


Fig.6

General scheme of plasmapheresis. Separation of the plasma from whole blood may be by centrifuge or membrane techniques. Plasma treatment may be by membrane filtration, sorption or other physicochemical techniques such as precipitation.

TABLE II

Implantable Vascular Access Devices*(14)

Company	Trade Name	Catalog No	Use	Internal Lumen of Catheter	Guaranteed Life of Septum	Approximate Price
Pharmacia	Port-A-Cath	550-400	Venous Kits	1.02 mm	(2,000 punctures w 22 ga	$295 – $350
Pharmacia	Port-A-Cath	550-350	Arterial Kits	.51 mm	1,000 punctures w 19 ga.)	
Pharmacia	Port-A-Cath	560-300	Arterial	.51 mm		$295 – $350
Infusaid	Infuse-A-Port	36583	Venous	1.00 mm	(2,000 punctures w 22 ga Special Infusaid Needle)	$250
Infusaid	Infuse-A-Port	36272	Venous or Arterial	.6 mm		$250
Cormed	Medport	50200	Venous or Arterial	1.00 mm	(1,500–2,000 punctures w 22 ga.)	$295
Cormed	Medport	50100	Venous or Arterial	.5 mm		$295
Cormed	Medport	50300	Venous	1.5 mm		$295

*Partial listing of Products Available per manufacturer's recommendations

TABLE III

Adult Total Parenteral Nutrition Solution

Base solution		
40–50% dextrose in water		500 ml
3.5%–10% crystalline amino acids		500 ml
Additives to each unit		
Sodium chloride, acetate, or lactate		40–50 mEq
Potassium chloride		20–30 mEq
Potassium acid phosphate (10–20 mM phosphorus)		15–30 mEq
Magnesium sulfate		15–18 mEq
Additives to any one unit daily		
Calcium gluconate 10%		4.5 mEq
Zinc sulfate		5–10 mg
Copper sulfate		1–2 mg
Iron–dextran		0.1 ml
Chromium chloride		10–20 mcg
Manganese chloride		0.5 mg
Selenium (sodium selenate)		60 mcg
Multivitamin infusion		10 ml
A	3300 IU	
D	200 IU	
E	10 IU	
Ascorbic acid	100 mg	
Folic acid	400 ucg	
Niacin	40 mg	
Riboflavin	3.6 mg	
Thiamine	3 mg	
B_6 (pyridoxine)	4 mg	
B_{12} (cyanocobalamin)	5 ucg	
Pantothenic acid	15 mg	
Biotin	60 ucg	
Additive to any one unit twice weekly		
Vitamin K		10 mg
Intravenous fat emulsion 10% or 20% 500 ml 2–7 times weekly		50–100 gm
Carbohydrate calories		850 kcal/liter
Protein calories		150 kcal/liter
Fat calories		1000–2000 kcal/liter
Nitrogen		6.5–8 gm/liter
Amino acids		40–50 gm/liter

TABLE IV

Pediatric Total Parenteral Nutrition Solution (31)

Base solution		
40% dextrose in water		500 ml
3.5% crystalline amino acids		500 ml
Additives		
Sodium chloride		25–30 mEq
Potassium acid phosphate		30–40 mEq
Magnesium sulfate		12–15 mEq
Calcium gluconate		25–35 mEq
Zinc sulfate		2 mg
Copper sulfate		0.5 mg
Iron-dextran		0.05 ml
Chromium chloride		10 mcg
Manganese chloride		0.25 mg
Selenium (sodium selenate)		30 mcg
Multivitamin infusion		10 ml
A	0.7 mg	
D	10 mcg	
E	7 mg	
K	200 mcg	
Ascorbic acid	80 mg	
Folic acid	140 mcg	
Niacinamide	17 mg	
Riboflavin	1.4 mg	
Thiamine	1.2 mg	
B_6 (pyridoxine)	1 mg	
B_{12} (cyanocobalamin)	1 mcg	
Dexpanthenol	7 mg	
Biotin	20 mcg	
Intravenous fat emulsion 10% 50–75 ml/kg 3–7 times weekly		
Infusion rate = 115 ml/kg/day		
115 kcal/kg/day		
3 gm protein/kg/day		

TABLE V

MODELS OF INFUSION PUMPS

Manufacturer	General Purpose	Microinfusion Purpose
ABBOTT	Life Care 3	
AMERICAN McGAW	Accu Pro	
AVI	Guardian 100	Guardian 100
CRITIKON	Simplicity 2100 A	
IMED	960	965
IVAC	560 1500	
TRAVENOL	Flo-Gard 8000 Flo-Gard 6100	
VALLEY LAB	Infutrol 6000b	Infutrol 6006b

TABLE VI

CONTINUOUS INSULIN DELIVERY SYSTEMS (24)

PUMP MODEL	MICROJET MC2-MC20	MILL-HILL 1001	AUTOSYRINGE	SYRINGEDRIVER MS26	CPI 9100	PROMEDOS E1
DISTINCTIVE FEATURE	Syringe	Syringe	Syringe	Syringe	Syringe	Peristaltic Pump
SIZE	17x7x2	14.4x6.9x3.3	18x8.3x2.5	16.7x3.3x2.3	14x8.3x2.4	11.4x6.5x2.7
WEIGHT (gr)	180	310	288	180	385	180
RESERVOIR CAPACITY	1-2 days	1-2 days	1-2 days	1-2 days	1-2 days	120 days
BATTERY LIFE	30 days	2 weeks	24 hours (accumulator)	30 days	1-2 days (accumulator)	2 months
ALARM	yes	no	yes	no	yes	yes
REASONS FOR ALARM SIGNAL	Empty reservoir Battery failure Pump runaway		Empty reservoir Battery failure Pump runaway		Empty reservoir Battery failure Pump runaway	Pump runaway

TABLE VII

feeding tubes for *Enteral Nutrition* [11]

	Material	Length	Gauge	Luer
Clinifeeding System 1 (Roussel)	PVC	80 cm	1 mm internal bore	Male
Clinifeeding System 1/85 (Roussel)	PVC	85 cm	1 mm internal bore	Male
Vygon Code 327	PVC	125 cm	6FG*	Male
Vygon Code 2327	Silicone	125 cm	6FG	Male
Duo-Tube (Argyle)	Silicone	102 cm	5/6/8FG	Male
Entriflex nasogastric tube (Searl)	Polyurethane Hydromer coated	93 cm	8FG	Female
Entron nasogastric tube (Searl)	Polyurethane Hydromer coated	91 cm	6FG	Female
Nasoduodenal tube (Portex)	PVC	105 cm	6–30FG	Female

*FG (French gauge) = external circumference in mm.

TABLE VIII-I

COMMERCIAL BLENDERIZED DIETS. NUTRITIONAL SUPPORT SYSTEMS [22]
(COMPARISON, 1000 CC STANDARD STRENGTH)

Product (Manufacturer)	Form	kcal	Osmolarity (mOs/kg)	CHO (g)	PRO (g)	FAT (g)	Na (mEq)	K (mEq)	Cl (mEq)	Fe (mg)	Ca (mg)	P (mg)
Compleat-B (Doyle)	L	1070	405	128 (48%)	42.7 (16%)	42.7 (36%)	56.1	38.8	24.5	12.0	667	1333
Compleat-Modified Formula (Doyle)	L	1070	Not available	141 (53%)	43.0 (16%)	37.0 (31%)	29.1	36.8	13.3	.12.0	670	980
Formula 2 (Cutter)	L	1000	435–510	123 (49%)	37.5 (15%)	40.0 (36%)	28.0	46.0	53.6	12.8	720	580
Meritene Liquid (Doyle)	L	1000	580 (Vanilla)	115 (46%)	60.0 (24%)	33.3 (30%)	39.9	42.8	47.0	15.0	1250	1250
Meritene Powder (Doyle) (as prepared with whole milk)	P	1070	680 (Plain)	119 (45%)	69.2 (26%)	34.6 (29%)	41.6	73.8	61.8	17.3	2306	1923
Nutri 1000 (Cutter)	L	1060	500	101 (38%)	40.0 (15%)	56.0 (47%)	23.0	39.0	Not available	9.4	1198	Not available
Sustacal (Mead Johnson)	P	1010	625	136 (54%)	61.2 (24%)	24.6 (22%)	40.5	55.6	38.2	18.9	1636	1363
Vitaneed (Organon)	L	1000	375	125 (50%)	36.0 (14%)	40.0 (36%)	21.5	32.0	24.0	9.0	500	500

TABLE VIII-2

COMMERCIAL BLENDERIZED DIETS. NUTRITIONAL SUPPORT SYSTEMS (COMPARISON/1000 CC STANDARD STRENGTH) (Continued)

Product (Manufacturer)	Carbohydrate	Protein	Fat	Flavors	Generic Description
Compleat-B (Doyle)	Hydrolyzed cereal solids, green peas, pea and peach purees, maltodextrin, orange juice	Beef puree, nonfat dry milk	Beef puree, corn oil	Unflavored	Meat-based blenderized tube feeding
Compleat-Modified Formula (Doyle)	Hydrolyzed cereal solids, green beans, pea and peach purees, orange juice	Beef puree, calcium caseinate	Beef puree, corn oil	Unflavored	Milk-based blenderized tube feeding
Formula 2 (Cutter)	Nonfat dry milk, sucrose, carrots, orange juice, green beans, wheat flour	Wheat, beef, egg, milk	Egg yolk, corn oil, beef fat	Orange	Oral or tube blenderized feeding
Meritene Liquid (Doyle)	Sweet skim milk, corn syrup solids, sucrose	Sweet skim milk, sodium caseinate	Corn oil	Vanilla, chocolate, eggnog	Supplemental or total diet
Meritene Powder (Doyle) (as prepared with whole milk)	Whole milk, nonfat dry milk, corn syrup solids	Whole milk, nonfat dry milk	Whole milk	Plain, vanilla, chocolate, eggnog	Supplemental or total diet
Nutri 1000 (Cutter)	Sucrose, lactose, corn syrup solids	Skim milk	Corn oil	Vanilla, chocolate	Oral or tube feeding
Sustacal (Mead Johnson)	Whole and nonfat dry milk, sucrose, corn syrup solids	Whole milk, nonfat dry milk	Whole milk	Vanilla, chocolate	Oral or tube feeding
Vitaneed (Organon)	Maltodextrin	Beef, sodium and calcium caseinates, vegetables	Soy oil	Unflavored	Blenderized tube feeding, low sodium, lactose-free

TABLE IX

Available plasma filters, membrane and module

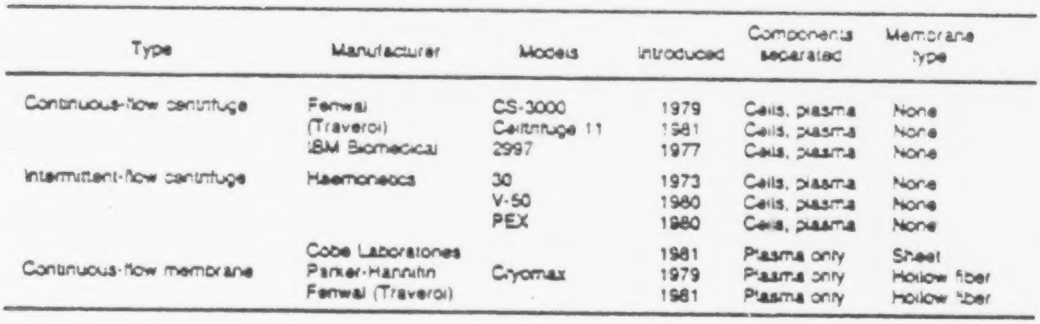
Filter	Type	Max. pore size (μm)	Material	ID (μm)	Wall thickness (μm)	Effective length (mm)	Effective surface area (m²)
Membrane							
Asahi Hi-05	HF	0.2	Cellulose diacetate	330	75	157	0.5
Kuraray PVA SA	HF	0.4	Polyvinyl alcohol	330	125	275	0.6
Toray Plasmax PS-05	HF	0.4	PMMA	370	85	175	0.5
Mitsubishi MPS	HF	0.2	Polyethylene	270	60	175	0.65
Fresenius Plasmaflux	HF	0.55	Polypropylene	330	140	200	0.5
Takeda separator	HF	0.55	Polypropylene	330	140	155	0.2
Travenol CPS-10TM	HF	0.55	Polypropylene	320	150	214	0.17
Teijin TP-50	HF	0.2	Cellulose diacetate base	330	75	150 (?)	0.5
Cobe Centry TPE	Plate	0.6	Polyvinyl chloride derivative	NA	—	NA	0.13
Terumo pile type	Plate	0.45	Cellulose acetate	NA	170	NA	0.4

	Priming volume (ml)	Container		Sealant	Sterilization method	Wet or dry
		Material	Dimensions LXϕ (mm)			
Module						
Asahi Hi-05	65	Polycarbonate	255 × 43	Polyurethane	Ethylene oxide	Glycerin, dry
Kuraray PVA	80	Polycarbonate Polypropylene	380 × 67	Polyurethane	Steam autoclave	Water, wet
Toray Plasmax PS-05	59	Polystyrene	240 × 73	Polyurethane	γ-Ray	Water, wet
Mitsubishi MPS	60	Polycarbonate	225 × 53	Polyurethane	Formaldehyde	Formaldehyde, wet
Fresenius Plasmaflux	54	Macrolon	250 × 50	Polyurethane	Ethylene oxide	Surfactant, dry
Takeda separator	21	Polycarbonate	245 × 56	Polyurethane	Ethylene oxide	Surfactant, dry
Travenol CPS-10TM	22	—	—	—	—	—
Cobe Centry TPE	—	—	—	—	Ethylene oxide gas	Dry
Terumo pile type	80	Polycarbonate	25 × 150	Silicone rubber adhesive	Ethylene oxide gas	Dry

HF, hollow-fiber; NA, not available; PMMA, polymethylmethacrylate.

TABLE X

Automated blood cell separation systems



Type	Manufacturer	Models	Introduced	Components separated	Membrane type
Continuous-flow centrifuge	Fenwal	CS-3000	1979	Cells, plasma	None
	(Travenol)	Celltrifuge II	1981	Cells, plasma	None
	IBM Biomedical	2997	1977	Cells, plasma	None
Intermittent-flow centrifuge	Haemonetics	30	1973	Cells, plasma	None
		V-50	1980	Cells, plasma	None
		PEX	1980	Cells, plasma	None
Continuous-flow membrane	Cobe Laboratories		1981	Plasma only	Sheet
	Parker-Hannifin	Cryomax	1979	Plasma only	Hollow fiber
	Fenwal (Travenol)		1981	Plasma only	Hollow fiber

TABLE XI

Diseases treated with therapeutic apheresis—plasmapheresis (plasma exchange)

Medical discipline	Protein-related	Antibody-related	Immune complex-related
Hematology	Waldenstrom's macroglobulinemia	Idiopathic thrombocytopenic purpura Factor VIII autoantibody Rh disease Autoimmune hemolytic anemia	Thrombotic thrombocytopenic purpura
Rheumatology	Raynaud's disease	Systemic lupus erythematosus	Rheumatoid arthritis Systemic lupus erythematosus Scleroderma Other
Neurology		Myasthenia gravis Multiple sclerosis Polymyositis Polyneuropathy	Guillain-Barré syndrome
Oncology	Multiple myeloma	Other cancers	
Nephrology		Progressive nephritis Glomerulonephritis Goodpasture's syndrome	Transplant rejection (?) Polyarteritis nodosa
Other	Toxins Poisons Hypercholesterolemia Thyrotoxicosis Primary biliary Cirrhosis Hypertriglyceridemia Hepatic insufficiency	Chronic active hepatitis Diabetes mellitus Pemphigus vulgaris Asthma	

TABLE XII

SECONDARY FILTERS

	Type	Max. Pore Size (μm)	Material	ID (μm)	Wall Thickness (μm)	Eff. Length (mm)	Eff. Surface. Area (m²)
ASAHI							
Cascadeflo	HF	-	CDA	200	30	130	1.7
KURARAY (Evaflux)							
2A	HF	-	EVA	200	50	190 230	1.0, 2.0
3A	HF	-	EVA	200	50	190 230	1.0, 2.0
4A	HF	-	EVA	200	50	190 230	1.0, 2.0
TEIJIN							
TA-100	HF	-	CDA	250	30	250	0.8
TA-200	HF	-	CDA	250	30	250	0.8
TERUMO							
CF-01	Plate	-	CA	-	110	70	1.0
TORAY							
AS-08	HF	-	PMMA	370	85	105	0.8
ASC-08	HF	-	PMMA	370	85	105	0.8

HF: hollow-fiber, CDA: cellulose diacetae, EVA: ethylenevinyl alcohol copolymer, CA: cellulose acetate, PMMA: polymethylmethacrylate

TABLE XIII

MACROMOLECULE REMOVAL BY ASAHI PLASMAFLO

	Amount Removed	Initial Concentration
Total Protein	22.3 ± 3.3 gm	6.2 ± 0.2 gm/dl
Albumin	12.1 ± 2.1 gm	3.5 ± 0.2 gm/dl
Globulin	10.1 ± 1.3 gm	2.7 ± 0.2 gm/dl
Fibrinogen	2,960 ± 550 mg	398 ± 93 mg/dl
Total Cholesterol	480 ± 140 mg	169 ± 28 mg/dl
Immunoglobulin G	2,640 ± 420 mg	803 ± 142 mg/dl
Immunoglobulin A	790 ± 130 mg	303 ± 104 mg/dl
Immunoglobulin M	620 ± 170 mg	284 ± 54 mg/dl
Immune Complexes	345,343 ± 381,123 U	600 ± 641 U/ml
Rheumatoid Factor	144,900 ± 23,900 RLS Units	208 ± 61 RLS Units/ml

TABLE XIV

Immunoadsorption systems described in the literature (72)

Immunoadsorbent	Substance removed	Application	Author
Protein A	IgG IgG immune complexes	In vitro	Rawer et al
Synthetic blood group B antigenic determinants	Anti-B antibodies	In vitro	Chang
Glomerular basement membrane antigen	Anti-GBM antibodies	Dogs	Terman et al
Bovine serum albumin	Anti-BSA antibodies	Dogs	Terman
Protein A	IgG	Dogs	Terman et al
Heparin-agarose	LDL	Dogs	Burgstaler et al
Anti-LDL-antibodies	LDL	Pigs	Stoffel et al
Glutaraldehyde treated human erythrocytes	Complement components	Sheep	Schmer et al
Heparin agarose	LDL	Sheep	Schmer et al
Staphylococcus aureus Cowan I	IgG	Human	Bansal et al
DNA	Anti-DNA antibodies	Human	Terman et al
Staphylococcus aureus Cowan I	IgG	Human	Ray et al
Blood group A and B antigen	ABO antibodies	Human	Bensinger et al
Anti-LDL antibodies	LDL	Human	Borberg et al
Protein A	IgG	Human	Terman

LEGEND OF FIGURES

1. Schema of blood access for TPN.(16)
2. Schematics of plasma separation by centrifugal and membrane devices
3. Principle of on-line membrane plasmapheresis. Separation of plasma from blood is achieved by utilizing membrane of 0.2-0.6 um porosity.
4. Scanning electron micrograph of membrane structure of various hollow fiber membranes. Left: Polyethylene (Mitsubishi 270H), Right: Polymethylmethacrylate (Toray PS-05).
5. Cross section view of hollow fiber type membrane plasma separator (Mitsubishi MPS-0165)
6. Structure of the Cobe plate-type membrane plasma separator
7. Filtration flux as a function of transmembrane pressure for plasma separators, and ultrafiltration by hemofilters and dialyzers
8. Classification of secondary filtration by temperature
9. Schematic of membrane plasmapheresis with on-line plasma treatment. Top: sorbent treatment, Middle: Cryofiltration, Lower: secondary filtration with recirculating flow, a process that differs from cryofiltration in the selection of filtering membrane and temperature of operation.

10. Cascade membrane technology for selective removal of macromolecules. General objectives for success of this technology are filter membranes of various porosities suitable for the selective removal of macromolecules from blood.

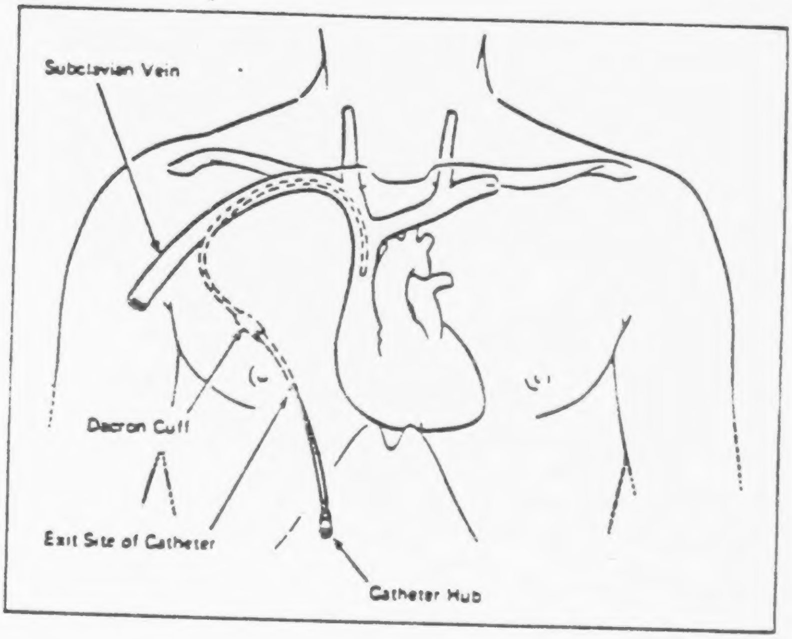


Figure 1

Schema of blood access for TPN(16).

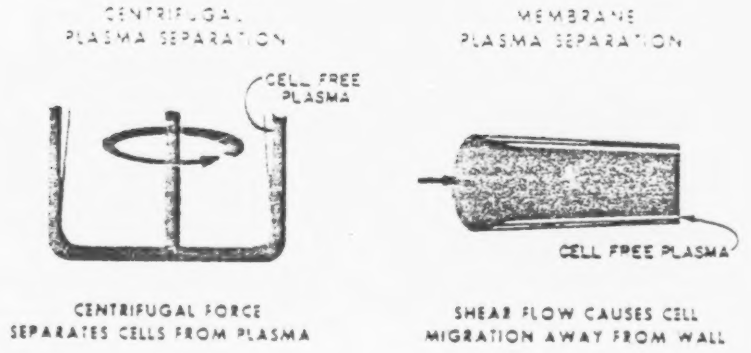


Figure 2

Schematics of plasma separation by centrifugal and membrane devices

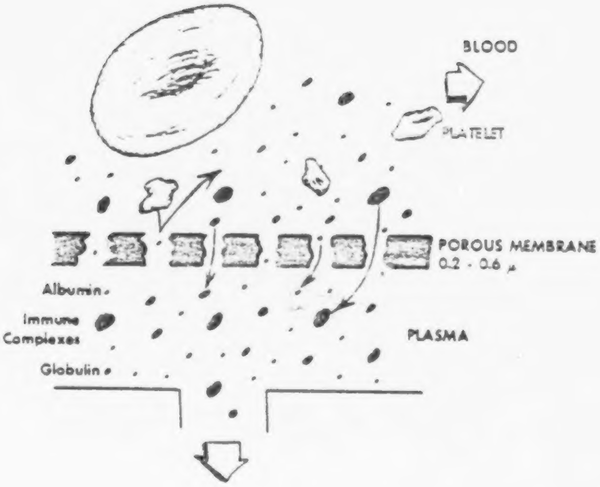


Figure 3

Principle of on-line membrane plasmapheresis. Separation of plasma from blood is achieved by utilizing membrane of 0.2-0.6 um porosity.

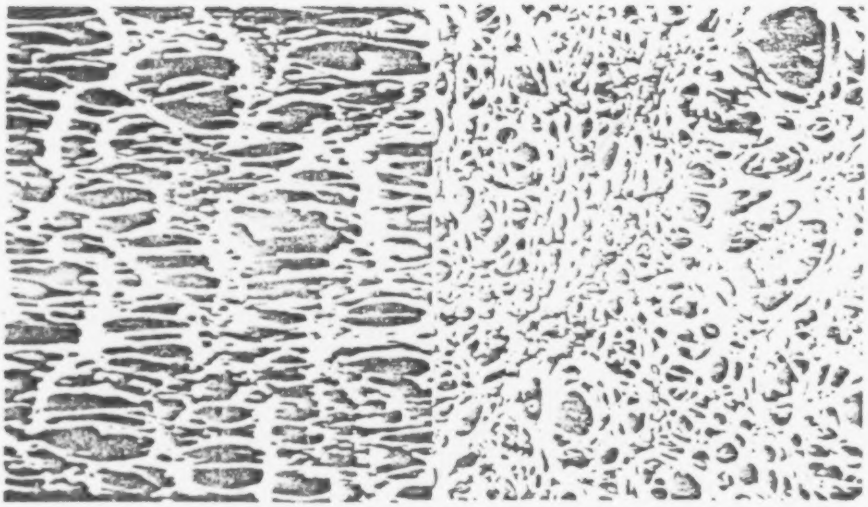


Figure 4

Scanning electron micrograph of membrane structure of various hollow fiber membranes. Left: Polyethylene (Mitsubishi 270H), Right: Polymethylmethacrylate (Toray PS-05).

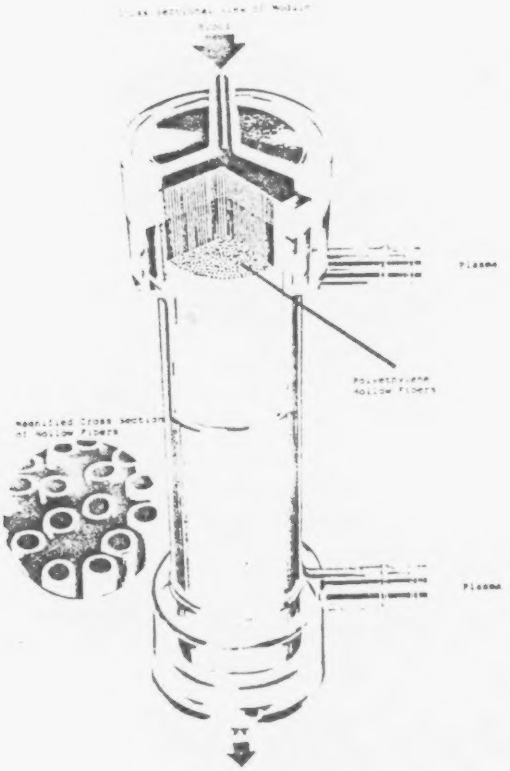

Cross sectional view of Module
Blood
Plasma
Polyethylene Hollow Fibers
Magnified Cross Section of Hollow Fibers
Plasma

Figure 5

Cross section view of hollow fiber type membrane plasma separator (Mitsubishi MPS-0165)

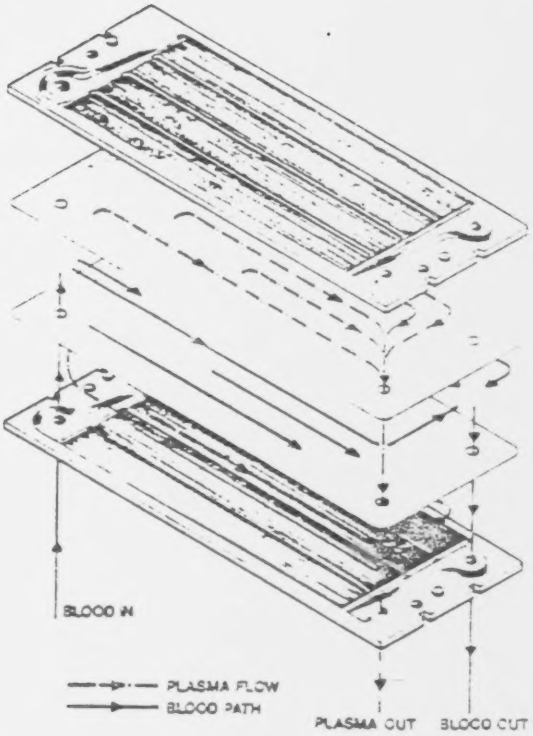


Figure 6

Structure of the Cobe plate-type membrane plasma separator

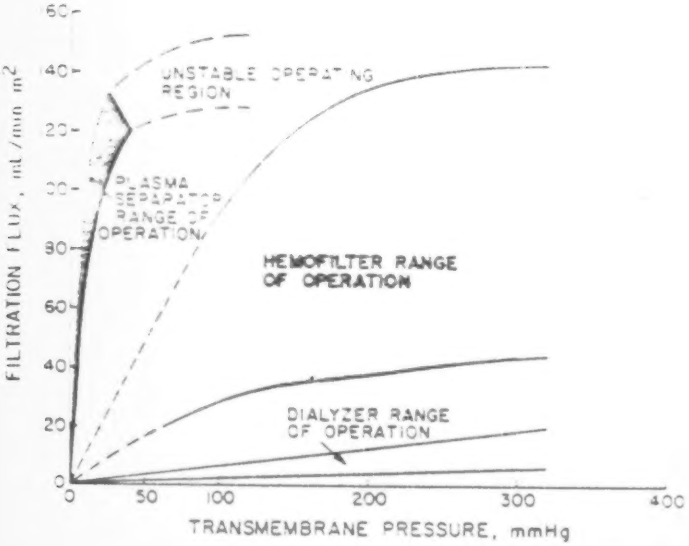


Figure 7

Filtration flux as a function of transmembrane pressure for plasma separators, and ultrafiltration by hemofilters and dialyzers

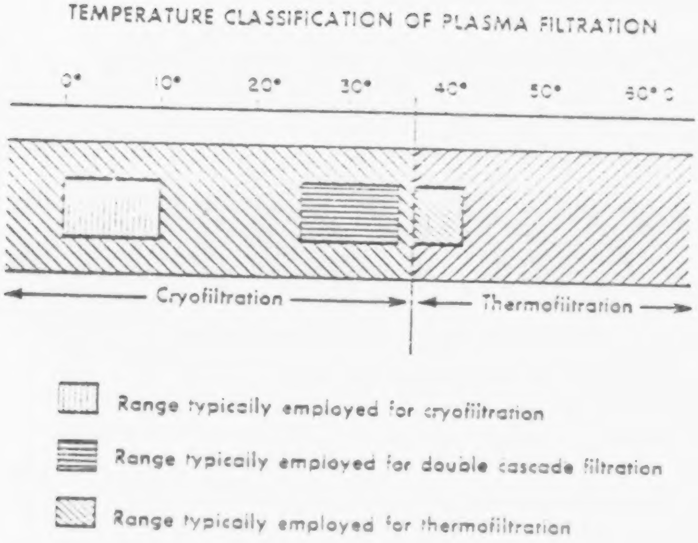

TEMPERATURE CLASSIFICATION OF PLASMA FILTRATION
0°
10°
20°
30°
40°
50°
60° C
Cryofiltration
Thermofiltration
Range typically employed for cryofiltration
Range typically employed for double cascade filtration
Range typically employed for thermofiltration

Figure 8

Classification of secondary filtration by temperature

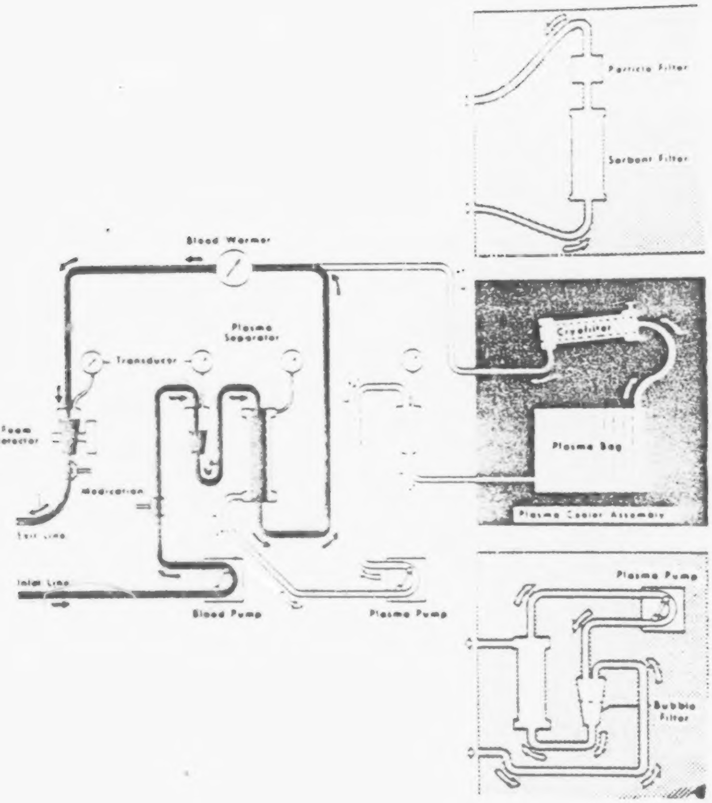


Figure 9

Schematic of membrane plasmapheresis with on-line plasma treatment. Top: sorbent treatment, Middle: Cryofiltration, Lower: secondary filtration with recirculating flow, a process that differs from cryofiltration in the selection of filtering membrane and temperature of operation.

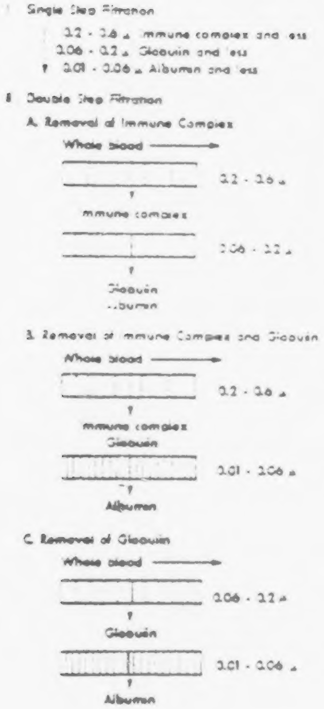


Figure 10

Cascade membrane technology for selective removal of macromolecules. General objectives for success of this technology are filter membranes of various porosities suitable for the selective removal of macromolecules from blood.

COSTS OF HUMAN GENOME PROJECTS

Tentative Meeting Agenda, August 7, 1987
Conference Room C/D, Office of Technology Assessment

9:00-9:30 Coffee and pastries

9:30-9:50 Introduction
    Opening statement and charge to panel.....Bob Cook-Deegan
    Chairman's preface......................Paul Berg
    Introduction of panel...................participants

9:50-10:30 RFLP Map
    average 1 centimorgan....................$
    average 10 centimorgan...................$
    associated infrastructure................$

10:30-11:30 Physical Map
    production of clones.....................$
    ordering.................................$
    repositories.............................$
    databases................................$

11:30-12:30 Technological Developments
    sequencing...............................$
    large fragment handling..................$
    automation and robotics..................$
    software.................................$

12:30-1:30 LUNCH

1:30-2:30 Organization
    advisory body............................$
    intergroup communications................$
    quality control..........................$
    personnel training.......................$

2:30-3:15 Other Costs................................$

3:15-4:30 Discussion: What are the implicit assumptions?

4:30 Summary and Concluding Remarks................Paul Berg

THE CLINICAL ECONOMICS OF NUTRITION SUPPORT SERVICES AND ANTIBIOTIC MEDICATIONS FOR THE CRITICALLY AND TERMINALLY ILL ELDERLY

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Henry Glick, M.A.
John M. Eisenberg, M.D., M.B.A.

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Prepared for the Biological Applications Program, Office of Technology Assessment, US Congress.

June 2, 1986

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I. INTRODUCTION

Concern about health care expenditures during the past two decades has led to a variety of policy initiatives, third party payer regulations and individual research efforts aimed at cost containment. Government and insurer efforts have usually concentrated on high unit-cost medical interventions such as inpatient days of care and high-technology services. Professional Standards Review Organizations (PSROs) were developed through the Medicare program and emphasized efforts to decrease unnecessary inpatient days of care. Blue Cross organizations designated hospitals that could maintain their own utilization review programs, also concentrating on unnecessary inpatient admissions and days of care. Second opinion surgery programs also emphasized high unit cost services to detect and prevent unnecessary ones. Efforts to limit the development of costly, high-technology interventions such as organ transplant programs, CAT scanner facilities and neonatal intensive care units were carried out through health systems agencies (HSAs) and the certificate of need (CON) process.

In contrast, many individual clinical investigators and medical care institutions concentrated their efforts on the use of less costly "little ticket" interventions such as laboratory services, radiologic examinations and the use of specific pharmaceutical products (1). A variety of approaches have been incorporated in these efforts, including education, administrative changes, penalties and rewards (2).

The success of these efforts to improve the use of medical care technology has been limited. Evaluations of PSRO programs, for example, indicate that little change in utilization occurred (3-5), and individual efforts also met with limited success. Efforts that have resulted in decreased use of services usually have been successful only in the short-term (1, 6). Other investigators (7) have found that the cost of instituting educational programs to change behavior outweighs the savings from decreased utilization.

The limited success of these government, insurer and individual programs may be related less to the rigor of the efforts than to the reimbursement environment that existed when the efforts were implemented. Until recently, cost-based systems were used to pay hospitals. All routine costs for inpatient days, costs associated with high technology interventions and expenses for low cost services were reimbursed by third party payers. This reimbursement system provided little incentive for hospitals to encourage the more efficient use of resources.

The recent implementation of case-mix payment programs such as those based on diagnosis-related groups (DRGs) for Medicare and Medicaid patients encourages hospitals to determine the most efficient use of resources. The predetermined fixed-payment is used to pay hospitals for all components of inpatient care, including routine costs, diagnostic services and therapeutic interventions. When more services are used during a hospitalization, the fixed payment is less likely to reimburse a hospital adequately for those services. However, when a lower level of intensity of services is delivered during a hospitalization, the fixed payment is more likely to cover the hospital's cost for these services. In environment, where the cost of individual services does not determine levels of payment, hospitals have an interest in identifying and encouraging the most efficient mode of care It is more likely that efforts to decrease the use of both high and low unit-cost interventions will be successful. It may be that previous programs that were unsuccessful in changing physicians' hospital practices would be successful in the environment of prospectively determined payment levels.

Medicare may modify the fixed payments that are made to hospitals by making periodic adjustments in payment rates. One method calls for adjusting payments for specific DRGs as changes in technology occur or as evaluations of inputs to care become available. Particular DRGs may be selected for review if the clinical efficacy of inputs to care is uncertain, if the individual DRG accounts for a large portion of Medicare outlays, or if unnecessary or inappropriate services seem to be used in caring for these patients. These efforts to adjust hospital payments encourage the use of technologies that have positive effects on clinical outcome for all patients, including severely ill patients, whose care may be particularly expensive.

This approach to adjusting expenditures suggests that care delivered to critically and terminally ill Medicare enrollees may be the subject of such evaluations, especially if their care is particularly expensive. A number of investigators have examined the proportion of Medicare payments allocated to individuals who died within a given time frame (see Section V of this report). Lubitz and Prihoda (8), for example, found that over one-quarter of all Medicare expenditures in 1978 were allocated to the almost 6 percent of Medicare beneficiaries who died in that year. Other investigators have found that the approximately 5 percent of Medicare beneficiaries who die in a year account for one-fifth to one-quarter of all Medicare payments (9-10).

When investigators have characterized high cost hospital patients, they have found that Medicare patients account for a substantial portion of these patients. Fleming and his colleagues (11) found that among discharges from 167 hospitals, 55 percent of the high cost patients were covered by Medicare. In addition, one out of ten Medicare patients was considered high-cost, and these patients accounted for 40 percent of the charges incurred by all Medicare patients discharged from these institutions.

Care delivered to critically ill patients is also likely to be scrutinized by hospitals and by Medicare because of the large capital investments necessary, such as those to build intensive care units or, to purchase high technology monitoring equipment. This scrutiny is particularly likely because of the equivocal evaluations of many interventions applied to critically ill patients. If the services are expensive but contribute little extra to the success of medical care, then the payor will not be interested in supporting them, and with prospectively-set payment levels, neither will the hospital be willing to pay for the services.

Two common medical care interventions, nutrition support services and antibiotic medications, are used frequently in caring for high-cost terminally and critically ill patients. Although the cost of these two services have been evaluated in several recent analyses, these evaluations usually have been limited to expenses for the specific service. The costs of side-effects and other related costs have not been carefully assessed, and expenses avoided by preventing adverse outcomes have not been fully examined.

This document reviews the techniques that are available for assessing the economic impact of medical care interventions, provides a critical review of the studies that have examined the financial consequences of the use of nutrition support services and antibiotic medication, describes how their economic impact may vary from different points of view, proposes the need for further studies and suggests policy implications of the available data.

I. ECONOMIC ANALYSES

Types of Costs

Illness and the medical interventions to diagnose and treat it consume substantial resources. Health economists have developed a classification system for the cost of these resources. Three types of costs - direct, indirect and intangible - are generally used to categorize these costs. The paragraphs below provide brief descriptions and examples of each type of cost.

Direct costs are the value of resources that could be allocated to other uses in the absence of disease (12). These direct costs are generally transactions for tangible products and services related specifically to the illness or to the provision of the medical care intervention, and include both direct *medical* and direct *nonmedical* costs. Medical costs for nutrition support services, for example, are generated by ordering the service (e.g., medical and clerical personnel costs), admixture preparation (e.g., solutions, equipment, pharmacy and nursing personnel costs), delivery (e.g., technician and supply or dispatch personnel costs) and the apparatus and labor for administration of the nutritional material (e.g., intravenous pumps and tubing, catheters, syringes and nursing costs). These costs may be incurred in different sites of care, including hospitals, ambulatory care programs and in-home medical care. Nonmedical costs occur as a direct result of the illness and its medical care, but these expenses are not medical in nature. They are other costs that are incurred because of the illness or the care of it. For example, travel costs to a physician's office or for family members to visit hospitalized inpatients, costs for special food items and expenses for homemaker services are all direct nonmedical costs.

Direct costs may be fixed, variable, or semifixed (alternatively called semivariable). Fixed costs do not vary with the volume of the medical service provided. For example, the salary of the director of the hospital pharmacy is not likely to vary with the number of total parenteral nutrition (TPN) solutions prepared. In contrast, variable costs are dependent on the volume of the medical intervention provided. For example, the cost of bottles of intravenous (IV) solution, IV lines and catheters are all variable costs.

Semifixed or semivariable costs have both fixed and variable components, in that they increase only after a substantial increment in services provided. For example, the cost of batch processing amino acids for five or ten bags of TPN solution includes storage of solution, which will not increase until the volume of services increases enough to require additional storage space. Then the storage costs will be fixed until another increase in the number of services provided is large enough to require still more space.

Distinguishing between fixed and variable costs is essential for calculating marginal costs, which should serve as the basis for decisions to change the volume of a medical intervention (or, for the clinician, to offer it to a given patient). Marginal costs are incurred by adding a unit of service or are saved by reducing a unit of service. Thus, the marginal costs of providing additional services in an existing program do not include capital acquisition, training and other fixed costs. Only the additional cost of providing the service, which may include personnel time for that one extra service and supply costs for that service, are included in assessing marginal costs.

It may be useful to distinguish marginal costs from *incremental costs*. Whereas marginal cost is a term that describes the cost of adding units of service to an existing program, incremental costs represent the costs of establishing a program. Using these definitions, a hospital that has no TPN program and is considering the establishment of one is facing incremental costs (for which the hospital hopes to have an incremental benefit). On the other hand, if the hospital already has a TPN program and the clinicians want to provide TPN to more patients, then the hospital faces marginal costs for which it expects to obtain marginal benefits.

Indirect costs are the costs of lost opportunities - such as the ability to earn income - that are due to morbidity and mortality. These costs are experienced by the patient, family, friends and society because of the lost patient's contribution to society. Indirect costs are incurred because of limitations on an individual's ability to continue his or her normal routine. One method of measuring these costs - the human capital approach - is to estimate foregone earnings due to morbidity and premature death. Another method of assessing indirect costs - the willingness to pay approach - relies on patients' reports of how much they would pay to reduce the likelihood of an adverse event.

Intangible costs include pain, suffering and other undesirable outcomes of illness that are difficult to measure directly. Investigators who assess these costs usually determine the frequency of the events, but rarely are able to assign costs to them. However, methods such as willingness-to-pay have been used to ascribe monetary values to the intangible outcomes.

Cost-Finding Methods

Direct costs of medical care may not equal their price because: 1) there are widespread imperfections in the medical care "market" (including cross-subsidies of services and lack of information about true costs upon which the calculated costs could be based), and 2) the point of view from which a study is conducted may affect the cost factors that are included in the analysis and the methods used to estimate the cost of the interventions. To address these issues, a number of methods have been developed to estimate costs, including component enumeration, cost to charge ratios and multiple regression techniques.

In component enumeration, the cost of an intervention is "built up" by summing the costs of its elemental tasks. For the first step of this method, a list is developed of the elemental tasks of each intervention. Second, the resources consumed for each component are estimated using techniques such as time and motion studies or activity diaries. These resource estimates are then multiplied by their cost (prices may be used if they are the true cost to the decision maker) to calculate the cost of each task in the third step. In the fourth step, the costs of all tasks are summed to calculate the total cost of an intervention (13).

Alternatively, cost to charge ratios use a top-down approach, starting with the charge for an intervention and adjusting it to estimate its true cost. This adjustment is usually made by multiplying the charge by the proportionate "mark-up" of costs in a department. In many hospitals, there is wide variation in the charges used by different departments. In part this relates to the way that hospitals allocate costs to different departments by an accounting algorithm called "step-down" accounting. However, it is also related to cross-subsidies by parts of the hospital that can generate income (e.g., pharmacy) to parts of the hospital that generate little or no income (e.g., social work department). To control for this variation in charges, the cost to charge ratios reported to the federal government in hospitals' cost reports may be applied to charges.

The third approach, *multiple regression techniques*, requires data on the variety of resources that are consumed (e.g, number of inpatient days, ancillary services, pharmaceuticals and nutrition support services) by a group of patients. Total cost data for these patients must also be available. Traditional regression techniques are then used with the volumes of the different services serving as the independent variables and with total cost as the dependent variable, to determine the contribution of each service to total costs. The y-intercept computed in the regression equation identifies the fixed component of total costs. The regression equation may also be used to determine the contribution of providing a unit of a specific service to total costs.

Types of Economic Evaluations

The results of economic evaluations of health care interventions may provide valuable information to policy-makers, hospital administrators and providers concerned with delivering medical care in an environment in which financial resources are constrained. There are three common types of economic evaluations: 1) cost identification studies; 2) cost-effectiveness analysis; and 3) cost-benefit analysis.

Cost identification simply requires that all the costs associated with an intervention be estimated and tabulated. Outcomes from the intervention are not assessed, the goal is limited to calculation of the cost of alternative approaches to patient care. This type of evaluation is valuable in determining the economic impact of an intervention on a hospital but does not consider its clinical effectiveness. It is also sometimes called a "cost-minimization" analysis because the goal is often simply to minimize cost among alternative approaches.

For cost-effectiveness analyses, an outcome is defined and the costs of achieving that outcome via alternative approaches are compared. The outcome may be lives saved, cases of disease prevented, or other relevant clinical outcomes, but it must be explicit. For example, a cost-effectiveness analysis might be conducted of the alternative approaches to maintaining patients' blood volume intraoperatively, such as transfusion, patient homologous transfusion, and donor transfusion. The cost of all ancillary services required by each method, the incidence and cost of treating any adverse reactions associated with each method, and the cost of obtaining blood would be summed. In addition, clinical outcomes would be determined, and the cost per unit of outcome for each intervention could be compared. Since many medical services have multiple outcomes (e.g., lives saved, cases detected or cured, improved quality of life, patient satisfaction), the determination of a single unit of outcome can be difficult. One approach to solving this problem is called utility analysis, in which the value of each outcome is assessed and the different values are added as units of utility.

Cost-benefit analyses require that all facets of the intervention, including the resources they consume and the value of the outcomes, also be measured in the same units, usually dollars. For example, the outcome of an intervention may be lives saved. In a cost-effectiveness analysis, the results would be expressed as dollars spent per life saved. In a cost-benefit analysis, the value of all resources consumed in providing the intervention and of the life saved would be expressed in dollars. The net cost or net benefit could be determined, thereby balancing the dollar value of the lives saved against the dollar cost of all resources used to provide that intervention.

III. NUTRITION SUPPORT SERVICES

National Expenditures for Nutrition Support Services

Nutrition support services are provided to approximately 15 percent of all hospitalized patients each year; 11.4 percent receive oral supplement services, 2.1 percent receive enteral feedings and 1.5 percent receive TPN. (14,15). In 1984, almost $1 billion was spent on TPN solutions and equipment, and $360 million was spent on enteral equipment and solutions. Including physician fees and administration costs, approximately $3 billion was spent on TPN for hospitalized patients in 1984 (15).

A number of investigators have examined the economic impact of nutrition support services - usually TPN and enteral nutrition (EN). However, the studies usually have been descriptive in nature and oriented toward one type of service in patients with specific diagnoses (16), have concentrated on pre- or postoperative nutrition support services (16-22) and have been limited to expenses for solutions and equipment. For inpatients, reports of the cost of per day solution and equipment per day range from approximately $150 (Canadian) to $485 (US) (17-18).

Expenses Related to Nutrition Support Services

Economic evaluations of nutrition support services have usually been limited to expenses for solutions and equipment. However, other components of providing nutrition to patients may also increase medical care expenditures, such as prolonged hospital stay, professional services and additional monitoring or diagnostic testing. Table 1 lists the components of these expenses. For example, in their trial of preoperative nutrition support for patients undergoing surgery for esophageal or stomach cancer,

	Component of Cost	Estimated Expense	Reference
1)	Solution and Equipment	a) $150/day b) $250-$185/day	a) 17 b) 18
2)	Insertion (one-time)	a) $200-$100/day	a) 18
3)	Laboratory Tests	a) $25-$210/day	a) 18
4)	Nutrition Support Service	a) $0-$140/day	a) 18
5)	Side Effects/Complications	a) $150-$275/day b) $0-$100/day	a) 17 b) 18

Table 1: Components of Total Additional Cost of Inpatient Total Parenteral Nutrition

Heatley and colleagues (23) performed periodic diagnostic testing of immune status and multiphasic biochemical testing of patients receiving preoperative TPN. Although expenses for this diagnostic testing were not enumerated, they may have been substantial, particularly since some patients were tested periodically for up to one year after discharge.

McArdle, et al, (22) also used additional laboratory tests to monitor patients' responses to parenteral and enteral nutritional support. They included laboratory tests of protein, albumin, ammonia, urea, glucose and total iron binding capacity determinations, and a variety of hormone assays. Of course, some of these studies may have included tests that were done for the purpose of research rather than patient care. It is difficult to know whether these costs would be incurred in typical practices. If they are performed outside of research studies for nonstudy patients receiving of nutritional support, they are costs that should have been included in an economic analysis of parenteral and enteral nutrition.

Twomey and Patching (18) do report expenses for factors other than solutions and equipment. Based on charge data from five California hospitals, they found that physician fees, radiologic examinations, laboratory tests and nutrition support team consultations constituted about 32 percent of the average total daily expenses for nutrition support services. Based on this charge information and the estimated number of patients receiving parenteral nutrition support (550,000) (14), national expenses for components of nutrition support other than solution and equipment may be as high as $89.1 million. Thus, these factors are important to consider in assessments of the economic impact of nutrition support services.

Steinberg and Anderson, in their report to the American Society for Parenteral and Enteral Nutrition, also list unpublished estimates of the cost of administering TPN from single institutions (15), ranging from $50 for solutions alone to $75 at a VA hospital, to $90 (Canadian) for solutions and labor at a Canadian hospital, to an estimate from a pharmaceutical company with a maximum of $400 per day, including lab tests. Estimates of the cost of providing enteral nutrition also included personal communications and ranged from $18-$30 per day.

Side-Effects

The development of side-effects and complications is another component of the cost of nutrition support that has received limited attention. Investigators who have addressed this issue usually have focused on catheter- related problems and, even so, have not examined the financial impact of these problems.

Miller, et al, (24) examined complications and side-effects that occurred in children receiving TPN during two time periods. The complications included catheter-related infections, metabolic complications such as jaundice and metabolic acidosis, and problems arising from solution administration (such as pleural effusion and venous thrombosis). In the latter data collection period, they found that 1.9 percent of patients receiving TPN experienced complications. Problems associated with administration of the solution accounted for almost all of the complications in the group receiving TPN by peripheral vein. Infections and metabolic complications accounted for most of the complications in the group receiving TPN by central vein. Increased expenses for these complications were not assessed by Miller and his colleagues.

Detsky and his colleagues (25) estimated the frequency of iatrogenic complications from both TPN and EN. Pneumothorax, air embolus, infection, and phlebitis, among others, were the adverse events included in the analysis of TPN. Complications of EN services included aspiration pneumonia, electrolyte and metabolic abnormalities and the dumping syndrome. Based on previously published studies, Detsky, et al, estimated that six percent of patients who receive TPN through a central line and three percent of patients who receive EN develop significant complications. These data were used in a decision analytic model of nutrition support services. However, no cost information was incorporated for the complications of TPN or EN in developing the decision tree.

Detsky and Jeejeebhoy (17) did include cost information in a later study. However, they assumed that the impact of iatrogenic complications of preoperative TPN would be limited to four days of hospital stay. Moreover, they estimated expenses for the prolonged stay to be $150 (Canadian) per day. Several elements of this study are unclear. For example, it is not clear which resources were included in arriving at this cost estimate; whether the occurrence of a complication would contribute to an increase in total length of stay; and whether true costs were used to arrive at the $150 estimate.

Twomey and Patching (18) assessed the impact of pneumothorax, systemic sepsis and subclavian vein thrombosis for patients receiving TPN through a central line. Based on charge data from a small sample of California hospitals, they calculated the charges per episode to be $1,400 for systemic sepsis, $830 for pneumothorax requiring chest tube insertion, and $200 for symptomatic subclavian vein thrombosis. They estimated average charges for the complications to be $12.50 per patient day during a ten day course of

TPN. Metabolic complications were not included because "(they) seldom generate major additional cost . . ." Other complications, such as air embolus and overwhelming sepsis, were also omitted because they occur rarely. Despite the low likelihood of these near fatal complications (e.g., air embolus), expenses for treating them actually may be very high. Therefore, the estimates of average per patient day charges for complications described by Twomey and Patching may be low since the high charges for treatment of these complications were excluded when per patient day charges were calculated.

Schattenkerk, et al, (21), in their study of post-operative nutrition support via needle catheter jejunostomy for patients undergoing laparotomy, found that 70 complications were experienced by the 210 patients. One-quarter of all patients experienced diarrhea and 3.3 percent of patients developed symptoms of ileus. Intraperitoneal leakage occurred in four of 210 patients. Although some cost data are reported, it is unclear whether expenses for treating the complications were included in these estimates.

Page, et al, (20) also examined the use of needle-catheter jejunostomy for providing postoperative nutrition support. Five complications (2.5 percent) occurred among the 199 patients. The catheter became dislodged for two patients, who subsequently underwent reoperation. Expenses for treatment of these complications were not included in the cost calculations.

Hinsdale and his colleagues (19) also examined the use of feeding jejunostomies in surgical patients. The overall complication rate was eight percent. These investigators also excluded expenses for treatment of complications from their cost analysis.

In an early study, Ryan, et al, (26), found that the complication rate was 4 percent among catheters placed and 6 percent among patients in the trial. The most common catheter complication was pneumothorax; the next most common was thrombophlebitis. Among the 355 catheters placed, catheter sepsis that was confirmed bacteriologically occurred in 20 cases. No economic analyses were included in this study.

Complications of nutrition support, particularly TPN, may be serious and require additional diagnostic services, therapeutic interventions, and inpatient days. Nevertheless, few investigators have included the additional incurred expenses in diagnosing and treating the complications, the true cost of the additional services, or the expenses for factors other than inpatient days.

Adverse Events Avoided by Use of Nutrition Support

In addition to the importance of assessing the total costs of the side effects of nutritional support, its benefits (especially with regard to adverse events avoided) should also be included in economic evaluations. A number of investigators have examined the incidence of postoperative complications in patients who have received nutrition support services and in those who did not receive any nutritional intervention. However, few have examined the economic implications of avoiding these adverse events.

Mullen and colleagues (27-29) report differences in complication rates among patients who received preoperative TPN and among patients who did not receive TPN. They considered complications such as sepsis and phlebitis, which are difficult to attribute definitely to TPN or to the surgical intervention. In general, however, patients who did not receive TPN perioperatively had a complication rate that was 1.5 to almost 3.0 times as great as that for patients who did receive nutrition support services.

In a small study of postoperative TPN and needle catheter jejunostomy, Muggia-Sullam (30) and his colleagues found no difference in the rate of surgical complications. No economic data regarding expenses for either therapeutic modality or adverse events were included in the report.

Twomey and Patching (18) acknowledge the methodologic deficiences of their approach, including using charges rather than costs, and combining data from several secondary sources to estimate the savings (benefits) from adverse events avoided with preoperative TPN for gastrointestinal cancer patients. They estimate that each wound infection avoided because of TPN saves $2,000 in treatment expenditures and that each major complication (e.g., death) avoided results in savings of $50,000.

Detsky and Jeejeebhoy (17) used decision-analytic methods to calculate the cost of postoperative complications avoided by a program of screening and administering TPN preoperatively. They conclude that from a pure cost-minimization perspective, no preoperative nutrition treatment should be undertaken for any group of patients, although testing patients for nutritional deficiencies and treating patients at risk reduced the postoperative complication rate. Therefore, while there were clinical benefits from preoperative nutritional therapy, there were no savings. However, the cost data used in these calculations seem conservative. For example, they seem to have assumed that patients experiencing postoperative complications would stay in the hospital for an additional 28 days. Moreover, they use the figure of $275 (Canadian) to estimate the average per diem expense for these days. It is unclear what treatment interventions and expenses beyond "hotel" costs were included in this estimate. Additionally, Detsky and Jeejeehboy do not state whether expenses were derived through budget allocations (as is applied in the payment of Canadian hospitals) or through a cost-identification effort. Another limitation of their study is that they assume that iatrogenic complications and nutrition associated complications are mutually exclusive.

Examinations of the economic impact of nutrition support services have not included thorough analyses of the potential savings from complications avoided. The economic value of these benefits may be substantial and may offset a portion of the expenses of nutrition support services. Well controlled, prospective studies have not yet assessed the incidence of the benefits and their true cost (the savings from avoiding complications) In addition, these studies have focused on surgical patients and have not examined adverse events avoided for other groups of patients.

Nutrition Support Services for Critically and Terminally Ill Elderly Patients

We were unable to identify any reports that focused specifically on nutrition support services for the critically and terminally ill elderly. Data from our instiution indicates that 21 percent (82 patients) of all Medicare patients who died in the hospital in fiscal year 1985 (July-June) (390 patients) received TPN or EN. Forty-one of these patients were on the Medicine service and 28 were on the Surgery service. The remainder were on the Gynecology, Neurosurgery, Neurology, Otorhinolaryngology, and Thoracic Surgery services. Thirty-seven of these patients were in the medical, surgical or neurologic intensive care unit during their hospital stay.

The average length of stay was approximately 41 days for the 82 patients who died and received TPN or EN and was 20 days for the 308 patients who died but did not receive these services. Average per patient total charges for patients who received TPN or EN were twice the charges for patients who did not receive TPN or EN. However, average daily charges (average total charges - average length of stay) for patients who received TPN or EN were only nine percent greater than the daily charges for patients who did not receive nutrition support services. Thus, these charges and length of stay may have reflected severe underlying disease which necessitated the nutritional support in the first place.

The reader should consider several factors and be cautious about the possibility of over-interpreting or generalizing the information presented above. First, the economic information is based on charges. As noted in Section II, charge data do not always accurately reflect the value of the institution's resources used to provide services. Moreover, charges do not reflect the Medicare payment to the institution for providing these services. Second, our institution is a large, urban, university-owned, teaching hospital. Several authors (31, 32) have suggested that patients cared for at teaching hospitals are more severely ill than their counterparts at nonteaching hospitals. Therefore, the use of TPN and EN, and length of stay at our institution may reflect the severity of illness among the particular patient population and not be generalizable to Medicare patients at all hospitals. Third, charges at a large urban teaching hospital may be greater than charges at other types of institutions. In fact, Eisenberg and Kitz (33) found that hospital charges for patients with osteomyelitis were two to thirteen times greater at two major urban teaching hospitals than at other hospitals. These differences may in part reflect differences in severity of illness within a diagnostic category, but also may reflect differences in both institutional charge structures as well as in the intensity of the care provided. As discussed below, charge data from one institution may be useful for raising issues for further investigation.

Policy decisions, however, should be based on cost information gathered from a representative sample of institutions.

Our analysis of the data presented by Steinberg and Anderson (15) lead to similar conclusions. Data from fiscal year 1984-1985 at Johns Hopkins Hospital indicate that of the 220 patients receiving TPN (excluding the 12 patients in DRG 468), 48 percent were in DRGs specifically designated for patients whose age was greater than 69 and/or who had complications or comorbidities (c.c.) Twelve percent of the total were in DRG 148 (major small and large bowel procedures age > 69 and/or c.c.), 10 percent were in DRG 154 (stomach, esophageal and duodenal procedures age > 69 and/or c.c.), four percent were in DRG 110 (major reconstructive vascular procedures without pump age > 69 and/or c.c.) and three percent were in DRG 442, (other OR procedures for injuries age > 69 and/or c.c.) These estimates of TPN use for elderly patients contain conflicting biases: they overstate use of TPN by the elderly, because, by using the number of people in the DRG, they include younger people who receive TPN and who qualify for the DRG by having complications and comorbidities rather than just people who qualify by being elderly. However, they also underestimate the number of elderly patients receiving TPN, because they do not count older patients who have conditions in other DRGs that do not have as one of their branching criteria age greater than 69.

As with the data from The Hospital of the University of Pennsylvania (HUP), average length of stay for Johns Hopkins patients was substantially longer for patients who received TPN than for those patients who did not. The mean length of stay for patients in DRGs 110 and 154 who received TPN were 45.2 and 41.5, respectively, while the mean lengths of stay for patients in these DRGs who did not receive TPN were 22.5 and 17.6, respectively. (Note, the average length of stay for TPN and non-TPN patients in DRG 148 was 26.6 and 25.4).

Similarly, although charges were substantially higher for TPN patients than for non-TPN patients ($27,190 vs. $13,522), this difference may be misleading. In an attempt to evaluate these differences, we performed a multiple regression analysis on the secondary data reported in Steinberg's and Anderson's report. We constructed a data set made up of three variables, the mean charges for each DRG, the mean lengths of stay for these DRGs and a 0/1 dummy variable representing whether the charge and length of stay information stemmed from patients who received TPN or those who did not. We weighted this data set using the number of patients receiving TPN in each DRG (e.g., because 8 patients in DRG 110 received TPN, we created 8 observations with the DRG 110 TPN patients mean charge and mean length of stay data and 8 observations with the DRG 110 non-TPN patient data; because 20 patients in DRG 154 received TPN, we created 20 observations with the DRG 154 TPN patient means and 20 observations with the DRG 154 non-TPN means). We first regressed length of stay (independent variable) on total charge (dependent variable); the R-square equalled .913, indicating that 91.3 percent of the variation in total charges is explained by length of stay alone. We then added the TPN dummy variable in a second regression, which only increased the R-square to .926, indicating that TPN adds little explanatory power to the prediction of total charges. We found it particularly interesting that the TPN coefficient was negative (-$3754; $p < .05$), indicating that TPN might even correlate with lower total hospital charges.

We feared that the T-statistics might be affected by the high multicollinearity between the length of stay and TPN variables (.74). To correct for this potential problem we transformed the TPN dummy variable to remove this correlation by regressing the length of stay variable on the dummy variable and then using the residuals from this regression in the total charge regression (this transformation assumes that TPN does not substantially affect length of stay). The relationships among the variables and the T-statistics in this regression remained consistent with those we uncovered in the second regression reported above.

One criticism that might be leveled against this analysis is that - as it is constructed - the length of stay variable assumes that all hospital days cost the same amount of money while conventional wisdom indicates that later days are less resource intensive than early days of hospital care. Thus, the negative coefficient on the TPN variable likely is reflective of the fact that TPN patients, who remain in the hospital longer than non-TPN patients, have smaller charges later in their stay. It does not, the critics would argue, indicate that TPN reduces the cost of hospitalization. Without more data, we cannot answer such a criticism; however, anecdotally we note that in the one DRG for which we have data where patient lengths of stay were similar for TPN (26.6) and non-TPN patients (25.4), total charges for TPN patients exceeded those of non-TPN patients by only $228 ($15,052 vs. $14,824).

The results of analyses of the HUP and Hopkins data suggest that the apparently excessive lengths of stay and charges that are associated with TPN may reflect differences in the severity of the underlying disease which necessitate the nutritional support in the first place. In neither case were we able to determine the additional costs that were the immediate result of nutritional support rather than reflecting these severity differences.

Several investigators have examined the use of TPN for patients who may be considered critically or terminally ill. Goodgame (34) reviews the literature regarding the use of TPN for patients with different diagnoses. He concludes that acute renal failure patients, a group that may be considered seriously ill, benefit from TPN and that TPN is an effective therapy for some of the complications of renal failure. The effectiveness of TPN in patients with hepatic failure is equivocal. With regard to TPN for cancer patients, Goodgame concludes that TPN is appropriate only when evidence of nutritional deficiency exists; he does not support its use prophylactically in these patients.

DeWys and Kubota (35) reviewed the technical aspects and clinical trials of nutrition support for cancer patients. They suggest that several studies have demonstrated the feasibility of administering TPN to cancer patients but have not reported on clear benefits of this approach. They also note that results of some controlled trials have demonstrated decreased complication rates for patients undergoing surgical therapy and increased tolerance to radiation and chemotherapy, while others have demonstrated decreased tolerance of therapy.

Payment For Nutrition Support Services

Inpatient: None of the available studies reports information about reimbursement for nutrition support services. Third party payer coverage is important to consider in estimating patients' out-of-pocket expenses for TPN and EN, and in determining whether payments accurately reflect institutional costs for providing the services. Currently, all three major third party payers (Medicare, Medicaid, Blue Cross) at our institution provide fixed-price payment for inpatient care. Therefore, institutional costs for TPN and EN services are not specifically reimbursed. In as much as expenses for these services were included in the historical data bases (1982 data) used to develop the fixed-price payment, institutional costs for TPN and EN are incorporated in the current payment levels. However, as Steinberg and Anderson (15) suggest, it is unlikely that any current fixed payment systems cover the hospital costs of patients receiving TPN.

First, as noted earlier, the Johns Hopkins mean charges for TPN patients in DRGs 110, 148, and 154 were $46,262, $15,052, and $32,914 respectively. The reimbursement weights for these DRGs are 3.3215, 2.9407, and 2.6880. Thus, even if Hopkins' reimbursement rate for a DRG with a weight of 1.0 had been $4,000 (far above the $3,000 average urban hospital rate), even if their charges had been significantly inflated, and even if there had been substantial outlier payments (outlier payments are generally relatively small compared with charges), two of these DRGs would have remained large reimbursement losers. Second, Steinberg and Anderson indicate that 33 of the 40 TPN patients at the Middlesex General Hospital, New Brunswick, New Jersey were outliers as defined by the New Jersey System and charges for six of the remaining TPN patients were substantially above the New Jersey DRG reimbursement rates.

Based on these data, Steinberg and Anderson have concluded that patients in need of TPN are at risk of losing this service. They base their conclusion on the premise that an underlying assumption of DRGs and other case-mix-based payment systems is that there is no identifiable type or category of patient who will tend predominantly toward being a gainer or loser; however, TPN patients do seem to be an identifiable group of losers, they suggest. Because, as has just been indicated, TPN is associated with high cost patients, they argue that "profit maximizing" hospitals will provide these patients with less costly, lower quality care. They posit three potential hospital responses:

a. total discontinuation of TPN at the hospital,

b. discouragement of physicians from using TPN, and

c. discouragement of admitting patients who might require TPN,

and argue that option (a) may be adopted because it will concomitantly fulfill option (c) and will allow the transfer of patients who need TPN.

We disagree that this problem is related to TPN; if it exists at all, it is generic to a case-mix-based reimbursement system. As we have already argued, it is unclear that TPN is causing TPN patients' high medical care costs; rather these costs seem to stem from the underlying severity of the patient's condition. Thus, if we assume that profit maximizing administrators actually exist (it can be argued plausibly that administrators base their decisions on the average return for a DRG or the average return for all DRGs), they will want to avoid treating these patients in their hospitals.

Steinberg and Anderson's argument likely would hold if the onset of TPN were the only signal that a patient was a high cost type. However, it is not. The same information that is used to determine if TPN is necessary can also be used to identify patients who are likely to lie at the upper end of the cost spectrum. Thus, if administrators are likely to behave opportunistically towards these patients, they will have the information needed to do so independent of a TPN program. Hence, an argument that administrators will respond by eliminating TPN programs depends on two underlying tenets: that the additional increment in costs resulting from the patient's receiving TPN will cause the administrator to act more opportunistically than he would if the patient's losses did not include TPN; and that the administrator's ability to deny admission or to transfer patients is significantly increased by the absence of a TPN program. We believe that TPN programs, per se, are not the problem; it is the patient's underlying ill health that may affect access to adequate health care.

Even if we are correct, some administrators may adopt the approach Steinberg and Anderson fear, and attempt to undermine TPN programs. One means of avoiding such an outcome is to adjust DRG-like payment systems to reimburse for TPN; however, this suggestion has the drawback that it may create incentives to place patients on TPN simply as a means of increasing reimbursement. This latter danger is enhanced because there are few well defined clinical criteria than can be used to judge whether TPN is appropriate therapy.

To overcome this problem, research should be targeted towards defining quantitative indicators for TPN use within a few selected DRGs. While some authors (15) have disagreed with the idea that these DRGs with high use of TPN can be identified, the fiscal year 1984 Johns Hopkins data indicates that 22 percent of all TPN was provided in DRGs 148, 154, and 468; 32 percent were concentrated in six DRGs (the three already mentioned plus 107, 110, and 204). In addition, while no denominator is presented, in 1983, the Cleveland Clinic provided TPN to 84 patients in DRGs 148 and and 154, and an additional 30 patients in DRG 149 -identical to 148 except for the age of the patient - received TPN as well (15). We conclude, then, that a strategy of targeting research into these DRGs is feasible. We note that adequate payment for a small set of DRGs with high use of TPN may have the concomitant advantage of providing incentives for profit maximizing administrators to retain TPN programs, thus making TPN therapy available to patients in DRGs that do not have additional reimbursement for TPN use.

Outpatient: Payment for services delivered in other settings should also be considered because terminally ill patients who are not acutely ill may be discharged to nursing homes or home, where they may continue to receive TPN. Members of the Department of Social Work at our institution indicated that Medicare patients who require TPN but who do not have supplemental insurance for nursing home care are "unplaceable" in nursing homes. Nursing homes do not receive supplemental payment for any of the equipment necessary for TPN. Major medical insurance, at least through Blue Shield, usually does cover TPN and EN services in the nursing home but require the patient or their family to pay a deductible and copayment.

Medicare covers the equipment, solutions, and nursing services used for home TPN, assuming the patients meet particular clinical criteria. To meet these criteria, a patient must have a diagnosis that is considered "severe pathology of the alimentary tract" and must be expected to require TPN for 90 days or more. Eighty percent of charges are reimbursed for supply, equipment and professional services for home TPN as part of the prosthetic device benefit program (personal communication, "Status of Medicare Home Health Coverage for Antibiotic Therapy and Nutritional Therapies," Health Care Financing Subcommittee, American College of Physicians, Spring, 1986). Medicaid coverage for home TPN varies by state. In Pennsylvania, such services may be approved on an individual basis. Major medical plans also cover these costs, although patients are responsible for deductibles and copayments. However, patients frequently are unable to meet this financial burden. Two home health care companies with which we spoke indicated that in order to meet regulatory requirements, home health care companies must bill patients for these copayments for two consecutive months. After that time period, home care providers may continue to provide services, need not bill patients for the copayments, but must absorb these expenses. These patient, family and corporate expenses for nutrition support services may create disincentives to discharging terminally ill patients who require TPN to nursing homes or home. Future studies should identify the factors that contribute to these expenses, the magnitude of these expenses and their impact on decisions to discharge patients.

In summary, estimates suggest that substantial funds are allocated to nutrition support services. However, these estimates rarely have included comprehensive assessment of all the components of delivery of nutrition support services, particularly for TPN and EN. Moreover, charge data rather than true costs have been used in these analyses. True costs are the value of the resources used in providing the services. Charges bear no consistent relationship to costs (36). In addition, components of total cost, such as direct nonmedical factors and indirect expenses, have not been included in these analyses. The limitations of the available data make it difficult to describe completely and accurately the economic impact of nutrition support services from the point of view of patients, insurers, hospitals or society-at-large. Further research is needed before accurate estimates may be made of the potential implications of policy intervention for nutrition support services.

IV. ANTIBIOTIC MEDICATIONS

National Expenditures for Antibiotic Medications

Approximately one-fifth of all prescriptions in the United States are for antibiotic medications (37). Nationally, about $3.5 billion is spent on drugs for hospital inpatients and 26 percent of the total, or $900 million, is spent on antibiotic drugs (38). Antibiotics also account for large portions of hospital pharmacy budgets. Kunin and his colleagues (39) found that antibiotics consumed 19 to 34 percent of the pharmacy budgets at three hospitals in Madison, Wisconsin. Cephalosporin antibiotics alone account for approximately 1 percent of hospitals' total budgets (40).

While these expenditures are substantial, results of studies that have evaluated inpatient antibiotic use have found that as much as one-half of the antibiotics were used unnecessarily. In an early study, Scheckler and Bennett (41) reviewed the charts of patients on surgical wards and found that 30 to 60 percent of patients receiving antibiotics had no evidence of infection. The authors postulate that the drugs were being used prophylactically against surgery-related infections. However, prophylaxis may be provided inappropriately. Gleckman and Gantz (42), for example, identified seven surgical procedures for which antibiotics are routinely used prophylactically despite a lack of controlled studies demonstrating the clinical efficacy of this practice.

The potential savings from eliminating the unnecessary use of antibiotics are large. Several authors have estimated that total spending on antibiotics could be reduced by about one-quarter to one-half if unnecessary use were eliminated (39, 42-44). Most of these estimates are limited to drug expenditures alone and do not include expenses for other factors that are important to consider in assessing the cost of antibiotic use. Some of these additional costs are described in the following paragraphs.

Costs of Administering Antibiotics

Estimates of expenses and potential savings from antibiotic use are conservative if they are limited to drug expenses. Other costs, such as those that are related to drug-administration, side-effects of treatment and adverse events avoided should also be considered in these evaluations (See Table 2).

Expenses associated with the administration of drugs are particularly relevant for hospitals that are paid by case-mix based systems, such as DRGs. Fixed-price case payment encourages institutions to identify and reduce their operating expenses, including personnel and supplies. These expenses (other than purchasing the drug) have not usually been included in economic evaluations of antibiotic medications.

Eisenberg and his colleagues (13) identified the components of hospital costs incurred in administering the drugs. They measured the cost of the non-drug variable elements associated with intravenous administration of cephalosporin antibiotics. Among the four hospitals studied, they found that the average variable cost per dose for delivering cephalosporins was $2.24. Nearly 60 percent of this cost was supply and material costs, which included syringes, alcohol swabs and other items for which the frequency of use varied with the frequency of drug administration. The other, approximately 40 percent of the variable costs, were personnel expenses. Nursing time for delivering and mixing the drugs, and pharmacy staff time for reconstituting drugs were included in these cost estimates.

In one of two similar studies, Tanner (45) estimated personnel and supply costs and found them to be $2.75-$4.48 per dose, depending on the specific parenteral system that was used. In the other, the Veteran's Administration Pharmacy Service Study Group (46) estimated that the average nondrug variable cost per dose at six Veterans Administration Medical Centers was $2.95 (ranging from $1.01 to $6.11 for the 16 different combinations of preparation and

Component of Cost	Estimated Expense	Reference
1. Personnel Time Reconstitution and Preparation, Delivery	a) $0.80-$1.09/dose b) $0.61-$0.86/dose	a) 13 b) 44
2. Supplies	a) $0.57-$2.08/dose b) $1.89-3.87/dose	a) 13 b) 44
3. Laboratory Tests	Variable with agent, diagnosis	
4. Solution	Variable with a antibiotic agent, nephrotoxicity	
5. Side Effects/ Complications	a) $238/case b) $167/patient day for nosocomial infections	a) 45 b) 47

Table 2: Components of Total Cost For Inpatient Antibiotic Therapy

administration that were studied). On a national basis, the findings from these three studies, when applied to total doses of comparable cephalosporins, indicate that $74-$233 million may be spent on preparation and administration of these parenteral cephalosporins alone. The three groups of investigators, in fact, found that total expenses for preparation and administration often exceed the purchase cost for drugs.

Adverse Reactions and Side-Effects

Side-effects of antibiotic treatment and adverse reactions to the drug are also important components of total costs but have rarely been included in economic evaluations of antibiotic medication use. Treatment for side-effects may require increased monitoring with additional laboratory tests, extended inpatient hospital stay and administration of additional medications. For example, ototoxicity and nephrotoxicity have been examined in relation to the use of aminoglycoside antibiotics (47). These investigators estimate that per patient expenses for patients who experienced nephrotoxicity were $238. However, these authors assumed that no patient would require renal dialysis and that there would be no increase in length of stay for patients who became nephrotoxic. Results of studies conducted in the 1970's indicate that expenses for renal dialysis were about $155 per session (48). Therefore, cost of renal dialysis for those patients with severe nephrotoxicity could add significantly to expenses for the side-effects and adverse events associated with aminoglycocide use. In another study of the cost of adverse events due to antibiotics, Kunin (39) points out that as the incidence of antibiotic-resistant infections increases, there will probably be an increase in the use of antibiotic sensitivity testing so that specific (rather than broad spectrum) and potentially more expensive, but also potentially less expensive, antibiotic therapy may have to be selected.

The development of antibiotic-resistant infections, which usually account for a large portion of nosocomial (hospital acquired) infections is an important side-effect to consider as a potential cost of antibiotic prescription. In 1974, the Centers for Disease Control estimated that five percent of all patients admitted to general hospitals acquired nosocomial infections (49).

Dixon (50) used data from the Comprehensive Hospital Infections Project and the National Nosocomial Infections Study to develop national estimates of the number of nosocomial infections, the impact of these infections on inpatient hospital days, and the financial consequences of the infections. He estimated that over two million nosocomial infections occur each year, that more than six million additional patient days are associated with treatment of these infections, and over one billion dollars in direct hospital expenditures are related to care of patients with nosocial infections.

A number of other authors have made additional estimates of the burden of hospital based nosocial infection. Freeman and McGowan (51) analyzed 85 pairs of patients, one with a nosocomial infection the other without, and found that these infections add 7.3 days to patient length of stay (2,000,000 x 7.3 = 14,600,000 excess patient days per year). Green, Rubinstein, and Amit (52) studied 57 pairs of matched patients and found that nosocomial urinary tract infections add 4.5 days to a patient's hospital stay, surgical wound infections add 11.9 days, and double infections add 25 days to the patient's stay (lower bound: 2,000,000 x 4.5 = 9,000,000 excess patient days per year; upper bound: 2,000,000 x 11.9 = 23,800,000 patient days per year). Finally, Spengler and Greenough (53) estimate that in their 81 matched pairs of patients, nosocomial bacteremia caused an excess of $3,600 in direct hospital costs; 24 percent of the total excess costs of the hospital patients with infections were preventable; and mortality rates were 14 times greater for patients with the infection than they were for those without the infection.

Nosocomial infections are also a serious problem in long-term care facilities for the elderly. In a study of a 432 bed Veterans Administration chronic care facility, Farber and his colleagues (54) found that UTIs had an attack rate of .22 infections per 100 patient days, Pneumonias were .19 per 100 patient days, and upper respiratory tract infections occurred at a rate of .18 per 100 patient days.

Magnussan and Robb (55) found an 18 percent nosocomial infection rate in a 400-bed Veterans Administration long-term care facility; 71.6 percent of these infections were urinary tract infections, 13.5 percent were respiratory tract infections, 11.1 percent were skin infections, and 2.5 percent were bacteremias. A survey of VA long-term care psychiatric facilities in the northeastern US had similar rates of repiratory and urinary tract infections (55).

Garibaldi, et al., (56) found that the prevalence of infections in a population of 532 patients in seven Salt Lake City skilled-care nursing homes was 16.2 percent. There were a total of six percent infected decubitus ulcers, 3.4 percent conjunctivitis, 2.6 percent sypmtomatic urinary tract infections, and 2.1 percent lower-respiratory-tract infections.

These infections induce treatment costs in the nursing home, and they also induce hospital costs. In a study of the causes of hospitalizations of 128 nursing home patients, Irvine, et al., (57) found that infections accounted for 27 percent of all these patients' hospital admissions. We estimate that the current DRG reimbursement rates for urban hospitals, standardized to remove the effects of labor markets and teaching status, are as follows: DRG 89 (Simple pneumonia age > 69 and/or c.c.) $3,500, DRG 277 (Cellulitis age > 69 and/or c.c) $2,637, and DRG 320 (Urinary tract infections age > 69 and/or c.c.) $2,567. Thus hospitalization for these conditions likely creates a heavy Medicare financial burden.

While wide-spread antibiotic usage certainly does not cause all nosocomial infections, it does tend to lead to the development of antibiotic resistant strains of infections and to superinfection in patients whose normal flora are altered. Thus, improper antibiotic use probably makes nosocomial infections both more common and harder and more expensive to treat.

Economic Evaluations of Antibiotic Use

Despite the widespread use of antibiotic medications and the economic impact of the use of these pharmaceutical agents, relatively few rigorous economic evaluations of antibiotic use have been conducted. The studies that are available concentrate on surgical prophylactic use of antibiotics, non-surgical prophylactic use of antibiotics, the appropriate use of these agents and on alternative modes of parenteral antibiotic therapy.

Surgical Prophylaxis: Stone, et al (58), conducted a prospective, randomized study of the use of prophylactic intramuscular cefazolin given to 400 patients undergoing elective gastric, biliary or colonic surgery. Patients were randomly allocated to one of three treatment groups or to a placebo group. The incidence of wound infections among the 200 patients who received the antibiotic preoperatively was four percent and 11 percent among patients who received the antibiotic post-operatively only or who received the placebo. The investigators also found that patients who had an incisional wound infection were in the hospital for over 15 days more than patients who did not have infections. Based on per diem charges, Stone and his colleagues calculated that excess charges for the extra inpatient days alone were over $12,000 per infected patient. Charges for the preoperative prophylactic antibiotic dose were $13.47 per patient. In this way, preoperative prophylaxis may prevent patients from becoming severely or critically ill and save hospital resources.

The economic aspects of using preoperative cefazolin for prophylaxis in patients undergoing clean vascular surgery were examined by Kaiser, et al (59). In a prior clinical study, they found an infection rate of 5.5 percent among 237 patients who received a placebo and no infections among 225 patients who received cefazolin preoperatively. Based on this clinical study, they calculated excess hospital charges for patients who developed a wound infection. These excess charges were $3600 - $8100, depending on the specific surgical procedure and the severity of the infection.

The costs and benefits of antibiotic prophylaxis for women undergoing abdominal and vaginal hysterectomies were evaluated by Shapiro and his colleagues (60). The economic evaluation was based on the results of a previous prospective randomized clinical study. In that study, investigators found that patients who received cefazolin had significantly lower infection rates than patients who received placebos in both vaginal and abdominal hysterectomy groups. Charge data from one hospital were used to determine the financial impact of the infections. The only factors included in the analysis were excess hospital days, microbiology cultures, antibiotic medications and extra physician visits for patients who received outpatient care. The investigators did not include expenses for extra medications or laboratory tests used to treat the infections. Results of the economic analyses indicated that per patient savings were $492 for vaginal hysterectomy patients and $102 for abdominal hysterectomy patients who received prophylaxis when compared with the placebo groups. Shapiro, et al, used national data about the annual number of abdominal and vaginal hysterectomies to estimate potential national savings from prophylactic therapy. They calculated that $100 million could be saved in a year if appropriate prophylactic regimens were used for vaginal hysterectomies and $40 million for abdominal hysterectomies.

The use of prophylactic antibiotics for patients undergoing appendectomy has also been evaluated (61). The wound infection rate was 9.6 percent among patients who received a placebo, but patients who received cefoxitin prophylactically had no infections. Hospital charges for excess inpatient days among patients with infections were $7,316 while charges for antibiotic prophylactic drugs were $2,884. On a per patient basis, savings of $84 could be achieved with the use of prophylactic cefoxitin sodium.

Busuttil, et al, (62) also examined the use of prophylactic antibiotics among patients undergoing appendectomy. Charge data were applied to excess hospital days, prophylactic medications and therapeutic antibiotics used to care for patients with wound infections. Charges were $96 less for patients who received cefamandole and carbenicillin and $248 less for patients who received cefamandole alone, when compared with patients in the placebo group.

Each of these studies found that the prophylactic use of antibiotics in surgical patients is justified from an economic perspective. Unfortunately, these studies usually were based on charge data, did not accoutn for differences in the severity of the patients' underlying illness, commonly limited antibiotic expenses to their purchase price and usually assessed expenses for infections by calculating extra days of inpatient hospital care. Critically and terminally ill elderly patients may be candidates for surgical prophylaxis, but these patients have not been particularly examined in these studies.

Nonsurgical Prophylaxis: Nonsurgical prophylactic use of antibiotics may be particularly relevant when considering elderly, terminally, and critically ill patients. Terminally ill cancer patients, those with compromised immunity, or those particularly likely to become infected may benefit from prophylactic antibiotics or from early empirical treatment of undocumented infections. However, economic evaluations of nonsurgical prophylactic use of antibiotics have not focused on these areas. Rather, studies have examined the use of antibiotics for prophylaxis of less serious infections. Nevertheless, the methods used in these studies may be used in studies of prophylactic antibiotic use against more serious infections.

Stamm and his colleagues (63) for example, conducted a cost-effectiveness study based on the results from their clinical study of prophylactic treatment of women with a history of urinary track infections. In that study, Stamm, et al, found that among women who had two or more infections per year, those who did not receive prophylaxis developed an average of three urinary track infections annually. Patients who received antibiotic prophylaxis only had 0.15 infections per year. Hospital charges for laboratory and radiologic services for other diagnostic services and for physicians visits were included in the analysis. Costs for drugs were also included. Expenses for prophylaxis were nearly $86 annually and expenses were approximately $490 for the treatment of patients who had infections and did not receive any prophylaxis, thus suggesting substantial savings from antibiotic prophylaxis.

Wong, et al, (64) also examined the economic aspects of treatment for urinary track infections. They included expenses for therapeutic agents, treatment of adverse reactions and treatment of infections in their analyses. Among patients receiving prophylactic treatment, expenses were $256 per year. Expenses for intermittent self-therapy were $239 per year. Each of these strategies was less costly than a 10 day antibiotic therapeutic regimen.

Alternative Modes of Antibiotic Care: Some economic evaluations of antibiotics have studied the potential savings from substituting outpatient for in-hospital parenteral antibiotic therapy. Poretz, et al, (65), estimated savings based on hospital room charges for inpatient days of care that were avoided for 150 patients aged 2-86 years with osteomyelitis and other serious infections. In another study, Poretz, et al, (66) administered questionnaires to 79 patients to assess costs for training patients to administer the antibiotics, supplies, professional services, inpatient days of care avoided (equal to duration of outpatient therapy), transportation (actual expenses or mileage x $.20) and lost days of work avoided (if hospitalized for antibiotic therapy). Average total cost was approximately $1,800 for outpatient care and average total benefits (excess inpatient expenses avoided) were about $6,600.

Stiver and his colleagues (67-68) have reported the results of their program designed to establish outpatient parenteral antibiotic therapy. Largely based on avoided inpatient days, they found savings of $97 per day for outpatient care when compared with inpatient parenteral therapy for a pilot group of patients aged 4-81 years with osteomyelitis, septic arthritis, infective endocarditis or other serious infection. Four years later they reported the results of a more comprehensive evaluation of the outpatient program. Expenses for outpatient care included visiting nurse services, other professional services, drugs and intravenous line supplies. Expenses for inpatient care included daily fees paid to Canadian hospitals and fees for physician services. Total savings were estimated to be over $315,000 for the 95 patients who underwent outpatient therapy.

Kind and his colleagues (69) reported on a small (14 patients) outpatient parenteral antibiotic therapy program for patients with osteomyelitis, endocarditis or septic arthritis. Based on charges for routine inpatient days and physician fees, Kind, et al, estimated per patient savings from outpatient care to be over $1,600.

Eisenberg and Kitz (33) recently estimated the potential savings from outpatient parenteral antibiotic therapy for osteomyelitis. They found that potential national savings are substantial, but that estimated savings are sensitive to the reimbursement mechanism used as the basis for calculating inpatient care expenses (the alternative mode of care). The variation in savings was related both to differences in the average length of stay for each source of data about length of stay and to differences in expenses for each source. Per patient savings from the early discharge mode of care varied from $510 to over $22,000.

The findings from these studies may be relevant for terminally ill patients who do not require acute care. Home parenteral antibiotic therapy may be a cost-effective way of delivering antibiotics for prophylactic or therapeutic purposes.

Methodologic Issues

Economic evaluations of antibiotic use have concentrated on four areas: surgical prophylaxis, nonsurgical prophylaxis, appropriate use and alternative site of care. Despite the scope of these efforts, there are methodologic weaknesses with most of these efforts.

First, most studies have used charge information to assess the economic impact of a treatment modality. For example, the studies that examined use of antibiotics in surgical prophylaxis used charges for inpatient days, pharmaceuticals, physician services and other factors to determine the economic impact of different prophylactic therapy regimens. The true cost of these factors was not assessed. Fixed costs were not distinguished from the variable costs that could be saved. Therefore, real savings to the hospital cannot be assessed. To determine the savings for third party payers, it would be necessary to have data on both the cost and payment rates for each service.

A second concern with these studies is that only charges for pharmaceutical agents were included in many of the studies. Hospital expenses for reconstituting drugs, for nursing time allocated to delivering the drugs and for supplies used in delivering the drugs usually were not assessed. The studies by Eisenberg, et al, (13), Tanner (45), and the Veterans Administration Pharmacy Service Study Group (46) indicate that labor and supply expenses for inpatient parenteral therapy may be substantial. Personnel and supply expenses were included in Poretz' earlier (65) evaluation of an outpatient intravenous antibiotic therapy program; per patient personnel expenses were approximately $150 and supply expenses were about $325. Additionally, except for Holloway, et al, (47) no studies comprehensively included side-effects in the economic evaluations.

A third issue is that these economic assessments usually were generally limited to direct medical expenses, including inpatient hospital days, pharmaceuticals, ancillary services and professional services. Nonmedical direct factors, such as transportation expenses by patients and their families and the indirect cost of time lost from work, usually were not included in these studies. However, results of studies conducted by Kind, et al, (69) (in which all patients returned to their normal routines) and Poretz, et al, (66) (in which 96 percent of patients were able to return to their normal routines) suggest that indirect costs may be relatively low.

A fourth issue is that studies usually have focused on inpatient hospital care. Potential cost-savings for care delivered in other settings, particularly nursing homes, is important to consider for Medicare and Medicaid. Approximately one million individuals (70), or 90 percent of all nursing home patients are over 65 years of age (71). Moreover, the severity of illness among these patients may be rising as hospitals discharge patients earlier in response to incentives created by the DRG-based payment program.

Antibiotic Medications Used for Critically and Terminally Ill Elderly Patients

Despite the recognition of antibiotic costs, the costs of their side-effects, the high cost of terminal illness, and the burden of disease in the elderly, there has been little specific attention to the cost of antibiotic medications for the critically and terminally ill elderly. Overall, however, elderly patients account for one-quarter of all expenditures for drugs and sundries while they comprise only 12 percent of the population (72, 73). Antibiotic use by nursing home residnets has not been well-studied, but may be particularly relevant because of the high proportion of elderly patients in this setting. From the point of view of insurers, it would be important to determine the extent of costs such as those incurred by unnecessary prophylactic use of antibiotics and the financial impact of side-effects of antibiotic therapy among elderly patients. Elderly patients may have a higher rate of multi-system disease, and also may be more likely to be susceptible to side-effects of antibiotic therapy than are other patients.

Payment for Antibiotic Use

In determining patient and insurer expenses for antibiotic use, it is important to consider the mechanism of payment for these services. For Medicare, antibiotic expenses for hospital inpatients are not particularly relevant since the DRG-based payment covers all inpatient services. This is also true for Medicaid programs in the states that have implemented DRG programs. At our hospital, these expenses are also irrelevant for patients covered by Blue Cross, which in Philadelphia also pays on a fixed-price basis, though not using DRGs. Patients are likely to bear a larger part of the financial burden of therapy as reimbursement policies incorporate higher copayment levels and higher deductibles.

Despite the apparent savings, outpatient parenteral antibiotic therapy is not usually included in third party payment programs. Poretz, et al, (65, 66) found that three private insurers who covered 20 percent of the patients, completely reimbursed the hospital for laboratory charges and paid the hospital 80 percent of charges for medications and supplies. However, the insurers only reimbursed the hospital for 80 percent of reasonable charges for all components of outpatient care. The local Blue Cross plan agreed to pay 100 percent of expenses for outpatient therapy after it was noted that patients would be unlikely to opt for this mode of care if they had to bear the financial burden of the difference between hospital charges and the reimbursement rate.

Kind, et al, (69) surveyed 18 insurance companies about their payment policies for outpatient antibiotic therapy. They found that (in 1976-1977) two local health maintenance programs would cover expenses fully, 14 private payers would reimburse 80 percent of expenses, and two payers - Medicare and a private payer - would not cover any expenses. Social workers at our institution also indicated that Medicare does not cover home parenteral antibiotic therapy, because it is considered a self-administered drug. Most Medicaid programs do provide payment (as per a fee schedule) for home parenteral antibiotic therapy, usually as part of traditional drug benefit programs. However, payment for equipment particular supplies, and professional services is problematic in some states (personal communication, "Status of Medicare Home Health Coverage of Intravenous Antibiotic Therapy with Nutritional Therapies," Health Care Financing Subcommittee, American College of Physicians, Spring, 1986). Major medical plans will usually cover 80 percent of expenses for these services, after a deductible is paid.

Information about third party payer expenses is important to consider in assessing the potential impact of cost-savings programs. Although outpatient parenteral antibiotic therapy may yield cost-savings for hospitals, patients may incur greater expenses if they must pay out-of-pocket for a portion of their outpatient care. Patients who may be reimbursed completely for inpatient care but only partially for outpatient care are less likely to select the outpatient mode of therapy. Terminally ill patients, who may be candidates for outpatient therapy, may avoid this mode of care because of its economic impact, regardless of the potential quality of life benefits.

V. DEFINING CRITICAL AND TERMINAL ILLNESS

Rigorous evaluations of the economic impact of medical care interventions require detailed descriptive information about the populations who actually receive or are candidates for the intervention. However, no standard diagnosis, clinical characteristic or therapeutic regimen has been established to define the concept of critical illness.

Investigators have used several approaches to define critical and terminal illness. One alternative has been to define critically ill patients as those who have intensive care unit stays or patients who have extended intensive care unit stays. Modoff, et al, (74), for example, focused on patients who were in the surgical intensive care unit for seven or more consecutive days. Almost 50 percent of patients survived to discharge from the hospital and one-third of all patients survived for at least one year after discharge. Unfortunately, no data are reported to indicate that the seven day stay criterion distinguishes between patients who have higher or lower expected survival rates.

Several factors make defining critical illness as that requiring intensive care difficult to apply in assessing the economic impact of health care technologies. First, it is not useful for prospective studies; extended intensive care unit stay can only be identified concurrently or retrospectively. Thus, patient populations for prospective economic analyses cannot be identified with this definition of critical illness.

Second, this method of defining critical illness does not distinguish between patients who require intensive care services for treatment of the most acute phases of a single disease and those patients who have multiple diseases that, together, require intensive care. This issue would also prevent investigators from examining the use of services in a well-defined patient poulation. For example, investigators might use this approach to identify patients for a study of parenteral antibiotic use among critically ill patients with pneumonia. However, if extended intensive care unit stay were used to identify patients (retrospectively), only patients with a diagnosis of pneumonia and patients with multiple diagnoses, including pneumonia, would be included. For these patients, it would be difficult to distinguish between services used solely to monitor and treat side-effects of the pneumonia, and antibiotic therapy and services used to monitor and treat the other diseases. Thus, the economic impact of the antibiotic therapy alone would not be assessed adequately.

Finally, intensive care is sometimes reserved for patients who are thought by the physicians caring for them to potentially gain from the intensive care unit. Some terminally ill patients are not transferred to the intensive care unit even if they have critical episodes, because the limited number of intensive care beds may be full or may be saved for more "salvageable" patients.

A second approach has been used by other investigators; letting high cost serve as a surrogate for critical illness. Fleming, et al, (11) defined high-cost as the top 25 percent of patients based on hospital charges among patients discharged from 167 hospitals across the country. Over 50 percent of these high-cost patients were over 65 years of age and, 10 percent of all Medicare patients were high-cost, accounting for 40 percent of total Medicare charges. This approach also requires retrospective analysis, does not adequately identify specific patient populations for economic studies and is sensitive to the charge-allocation procedures used by individual hospitals. Particular services may be "overcharged" at an institution and patients who receive these services may be identified as critically ill, regardless of their clinical condition.

Kobrinski and Matteson (75) used a threshold of $4,000 in hospital charges to identify high cost patients. Among their sample of patients discharged from 58 hospitals in 1977, 6.6 percent were considered high cost. Nearly one-half of the high cost patients were covered by Medicare.

Schroeder, et al, (76) characterized patients who had yearly hospital charges that exceeded $4,000. Depending on the sponsorship and teaching status of the institution, 4-24% of patients discharged met this criterion. Over 13 percent of all high cost patients died in the hospital during the year.

Berki and his colleagues (77) characterized the top 5 percent of patients based on charges among all patients discharged from a large group of hospitals. They found that approximately 45 percent of all patients over 65 years of age were considered to be high cost patients.

Robert A. Harootyan, writing for the Office of Technology Assessment (Robert A. Harootyan, OTA, February, 1986), uses the following definition of critical illness: "Critically ill patients are those who are experiencing serious physiological dysfunctioning, often with multiple diseases that present themselves in unusual or unexpected patterns. These patients are highly likely to be on a downward trajectory, to have lowered physiologic reserve, and to suffer from complications of treatment regimens, thereby reducing certainty regarding life-and-death outcomes and making treatment decisions more complex and difficult." (p 2-48). This definition of critical illness does consider a variety of factors in identifying a group of patients. However, no explicit criteria are available to identify "lower physiologic reserve," "serious physiologic dysfunctioning" or "downward trajectory," and the definition does not lend itself to operational application without further definition of the terms and the review of a large number of hospital charts. Hospital data bases could be used to limit the number of cases reviewed, but not to identify the critically ill patients.

Whereas critically ill patients require highly intensive, acute care services regardless of their likelihood of survival, terminally ill patients are expected to die within a given time period, regardless of the intensity of services delivered. Although we would seek a more clinically relevant definition for terminal illness, one that would reflect the biologic phenomenon, no single, widely-accepted set of characteristics is used to identify terminally ill patients. Bayer and his colleagues (78) recognized this problem in their discussion of the use of limited resources for terminally ill patients. They note that "though widely used, it [terminal illness] is not a standard technical term with clear and precise criteria" (p. 1491). Although some definitions use "a high likelihood of imminent death," the probability that defines "high likelihood" and the duration of "imminent" are not established. The Office of Technology Assessment uses six months as the time period in which death is expected.

Spector and Mor (79) used death certificates to identify patients in a study of charges generated by cancer patients. As discussed above regarding intensive care unit use to identify critically ill patients, this approach is only useful for retrospective studies of patients who died. This approach does not facilitate prospective studies of patients likely to die within a given time period.

Scitovsky (80) notes that this approach of retrospectively identifying expenditures for patients who died necessarily identifies expenditures for patients who were clearly terminally ill. Patients who died are often selected for the analyses, without comparison to costs for patients with similar diagnoses and severity of illness who lived. Therefore, this approach yields information about the cost of dying, but not necessarily the cost of being terminally ill. Scitovsky's review of information about Medicare enrollees indicates that more than five to six percent of Medicare enrollees die in a year and account for about one-fifth to one-quarter of all Medicare expenses.

The lack of explicit criteria to identify terminally ill patients also compromises efforts to examine the economic impact of health care interventions for this group of patients. For example, particular interventions may delay death in a small portion of a group of gravely ill patients, most of whom are expected to die within a given time period. By excluding the people who survived from the analysis, the additional direct medical and direct nonmedical expenses incurred by these patients would not be included as a cost associated with the intervention. In addition, any direct or indirect costs avoided (benefits) from extended life would not be included in the analysis.

In essence, no clear-cut, widely used definitions for critical and terminal illness are available. Critical illness has not been explicitly defined, and high cost or intensive care unit use often has been used as a proxy measure. Because it is difficult to predict accurately which patients are likely to die within a given time period, terminal illness is usually assessed retrospectively from the time of death. To assess accurately the economic impact of antibiotics and nutrition support services for critically and terminally ill patients, definitions must be developed that allow prospective identification of these patients according to explicit criteria. Otherwise, the assessments may be highly dependent on modes of care at different institutions (e.g., use of intensive care services), may not be specific to the use of an intervention, and may not clearly be applicable to a defined patient population.

VI. IMPACTS FROM DIFFERENT POINTS OF VIEW

In assessing the economic implications of health care interventions, it is important to consider the point of view from which the analysis is conducted. The point of view reflects the group whose resources are being consumed, and the relative impact of this resource consumption given the total resources available. Four points of view - those of patients, providers, third party payers and society - may be considered in these analyses.

Often the point of view is also that of the decision maker, but frequently the provider (doctor or hospital) makes the decision while the patient or third party payer is the one whose limited resources are being used. Ironically, a cost for the patient or third party payer may actually be income for the decision maker. Ideally the physician will make the decision, in large part on behalf of the patient. If the physician is also concerned about societal expenditures for medical care, he or she will be in the difficult position of making a decision by considering the patient's viewpoint as well as his or her own and that of society. In some cases the doctor may also be expected to take the perspective of the hospital or the third party payer into account. The necessity for the physician to consider several viewpoints simultaneously means that conflicts of interest are inherent in clinical decision-making.

Considering the point of view is important for four reasons. First, the components of total cost that are incurred by each group are different. For example, direct nonmedical expenses for transportation and homemaker services are important to patients. Hospitals, however, do not incur expenses for these factors and may not be concerned with their cost. In addition, third party payers rarely cover direct nonmedical expenses and thus will be unconcerned with expenditures for transportation and homemaker services. From the point of view of society, direct nonmedical costs are important; expenditures for these factors contribute to the nation's expenditure of resources related to illness and medical care for it.

The second reason to consider the point of view that has been selected for an economic analysis is that the actual cost may differ from different points of view. For example, patients covered by Medicare will not incur any additional expenses for inpatient antibiotic drugs because they are included as part of the DRG payment. From the hospital's point of view, the cost of the drugs includes expenses for personnel, salaries, employee benefits and training, pharmacy equipment and purchase of the drug. From the insurer's point of view, the cost of the drug is the reimbursement paid for these services. From the point of view of patients not covered by Medicare, the cost of the drug is the amount of money the patient must pay for it. From society's point of view the cost of the drugs is any resource that is consumed in its provision (similar to the hospital's cost) plus costs incurred by other parties (e.g., patients receiving outpatient drugs who incur nonmedical costs).

The third reason for considering the point of view is that different data are needed to use the findings from specific studies to estimate expenditures on a national level. For example, certain epidemiologic data such as the number of individuals expected to receive an intervention and the socioeconomic and clinical characteristics of the patient population would be needed to estimate societal expenses. On the other hand, to estimate expenses for all patients, the necessary data would include factors such as patients' third party coverage, employment status, length of hospital stay and expenses for direct nonmedical services.

Fourth, the policy implications that may be drawn appropriately from evaluations will also vary with the point of view used in the evaluations. For example, it may be inappropriate to use the results of an economic evaluation conducted from the patient's perspective to develop policies for hospital administrators. Patients fully covered by medical insurance will not themselves incur expenses for hospital care. Thus, for example, the results of an evaluation of the cost of a prophylactic antibiotic coverage from a patient's point of view, would not include covered hospital costs.

The following paragraphs present details about the elements of total cost that are relevant for each point of view, the cost of these elements, the data needed for economic evaluations and the potential policy implications. Understanding each point of view is important for evaluating studies that have been conducted, for designing future studies and for identifying priority areas for future research.

Patient Point of View

The elements of total cost that are likely to be important to patients are direct nonmedical factors, insurance co-payments and time lost from work (indirect expense). Patients who do not have health insurance or other coverage will also be concerned about direct medical care factors, which are charges and represent patients' out-of-pocket costs. Foregone wages are patients' indirect expenses.

To conduct a thorough economic evaluation of a health care intervention from a patient's perspective, a diary or questionnaire could be administered regarding patients' direct nonmedical expenditures. For example, transportation to and from the hospital, and to a provider's office for ambulatory care could be included in this questionnaire. Similarly, information about a patient's employment status, sick leave policies and salary would be important to calculate foregone wages.

Hospital Point of View

From a hospital's point of view, the relevant cost components are generally related to direct medical care factors. In particular, routine inpatient days, intensive care days, operating room time, pharmaceuticals, ancillary services and staff professional services (e.g., social workers, physical therapists) would be important considerations for hospitals. The volume of services used would be dependent on the intervention itself as well as on the secondary effects of the intervention such as adverse outcomes that require further diagnostic and therapeutic measures (leading to additional impatient days for example).

True costs to the hospital for these factors would include the additional personnel expenses allocated to delivering the additional routine days of care as well as the additional specific services. Supply costs and expenses for overhead factors such as heat and light, capital depreciation and administration salaries would also be included in the cost calculations, but only if the hospital's overhead is influenced by the clinical decision being evaluated.

To conduct an evaluation from a hospital's point of view, data are necessary about the number of patients receiving the intervention of interest and the hospitals' services consumed by these patients. These data might be collected through retrospective chart review to identify the services used by patients. Cost data would be applied to the volume data. Alternatively, concurrent prospective service utilization and cost-finding efforts could be conducted.

Third Party Payer Point of View

For third party payers, the economic impact of a health care intervention may be assessed by gathering data regarding the number of subscribers expected to receive the intervention. Data on payment rates for specific services would be used to assess insurer costs for these services. For Medicare and other third party payers who have implemented case-mix-based, prospectively set levels of payment, specific services used during the course of hospitalization are of interest in that they may influence the hospital's cost, but they do not influence the cost to the third party payer, at least in the short term. In the long run, insurers may adjust the fixed payment rates if historical data about costs are used to determine payment rates, or if services used for those patients have been found to be unnecessary or inappropriate.

Societal Point of View

From the point of view of society as a whole, any resource that is consumed or opportunity to produce that is lost represents a cost. Therefore, the true cost of providing inpatient care (which is also important from the hospital's perspective), out-of-pocket costs to the patient, and indirect costs would all be available for alternative uses. Therefore, the opportunity to use them for alternatives is lost and a cost is incurred. From the perspective of society as a whole, its options are more limited because of the resources having been consumed or because the individual's contribution to the economy has been foregone.

VII. ETHICAL ISSUES

Rationing

Decisions to limit resources for health care require that health care services be rationed at some level. On a national level, the proportion of a country's income used for health care may guide decisions about the proportion of funds allocated to technology development, research support, capital investments and therapeutic interventions. At the level of medical decision-making, data about cost, benefit and effectiveness may increasingly become part of the calculus of clinical practice.

In their examination of health care resource allocation decisions, Aaron and Schwartz (81) compared spending for health care services in Britain and the United States. At that time about 10 percent of the gross national product (GNP) of the United States was spent on health care while just over five percent of Britain's GNP is allocated to health care. Moreover, in Britain, the national government determines the funds that will be allocated to health care and to what categories of health spending they will be applied. Additionally, health care funds are allocated differently in the two nations. In the United States, for example, almost 70 percent of all health care expenditures are for direct health care services such as hospital care and physician visits. Thirty percent of expenditures are for capital, research, administration and other non-service factors. In contrast, Britain allocates 93 percent of expenditures to direct health care services. These data suggest that the United States has placed a higher priority on research and facility development than has Britain. Britain also allocates relatively more funds for hospital care than does the United States. Fifty-six percent of per capita expenditures in Britain are for hospital care, while 38 percent of per capita expenditures are for these services in the United States (81).

Societal Issues

Decisions to ration services, particularly by witholding them at the clinical level, are difficult in the United States where providing additional services has been encouraged and has come to be expected. This parallels physicians' usual training to do whatever is necessary for diagnosing or treating patients. Thus, all parties participating in decisions about service delivery have traditionally encouraged increased use of services in the United States. However, particular services, including out-of-hospital parenteral therapy (e.g. nutrition, antibiotic, cancer chemotherapy), have not been routinely covered by health insurance programs. Thus, the use of these services in the outpatient setting has been inhibited without regard to the clinical appropriateness of the service.

Hospital Issues

The societal decision to ration services is often implemented at the level of the provider. Butler and his colleagues (82) examined length of medical intensive care unit stay, DRG, and clinical course for all patients cared for in the intensive care unit at their hospital during the period of July 1, 1982-June 30, 1983. They estimated DRG payments for these patients, including base-payments, pass-through expenses, indirect education expenses and outlier payments in their estimates. Butler, et al, went on to assess costs of care by applying Medicare cost-to-charge ratios to patients' billed charges. Calculated costs and DRG reimbursement rates were compared and losses were estimated. Overall, in one year, 446 Medicare patients who received medical intensive care generated an estimated loss of $4.7 million dollars for the hospital. According to the authors, the findings suggest that "extensive utilization (of medical intensive care) will jeopardize the financial viability (of hospitals)." These losses from DRG payment force internal management decisions regarding capital investments in monitoring equipment, nurse staffing for intensive care units and monitoring of physicians' use of intensive care services. Fewer resources may be devoted to delivering intensive care, particularly if financial factors serve as the basis for these capital allocation decisions.

Butler and his colleagues (82) also suggest that it is important to assess factors such as the cost-effectiveness of intensive care units before fully-informed management responses to changes in reimbursement can be formulated. Similarly, economic evaluations of other specific medical care interventions are important for hospital management or medical decisions about the use of these services.

From the hospital's perspective, specific interventions such as nutrition support services and antibiotic medications are farther removed from administrative control than are intensive care units. Little capital investment, which is usually under administrative control, is required for these services. Once the service has been established (e.g. parenteral nutrition), administrators have little control over their cost. Rather, it is the intensity of the use of these resources and the operational costs they generate that are key to control hospital expenditures. This may be achieved by increasing control over hospital formularies, support for pharmacy and nutrition support services and criteria-setting regarding site of service for specific interventions (e.g., only outpatient long-term TPN). On the other hand, administrators may encourage the use of specific resources if their use is associated with decreased lengths of stay and lower complication rates (i.e., cost-benefit ratio is favorable). To control the utilization of these specific resources, hospital administrators will increasingly want to influence physicians' more directly. The independent nature of physician decision-making may be threatened as hospital administrators carefully examine these decisions.

Physician Issues

In this changing environment, Eisenberg (83) points out that physicians are being asked to make decisions that implicitly incorporate assessments of the cost-benefit or cost-effectiveness of individual medical care interventions. Levinsky (84) suggests that physicians' decisions should be based on what is best for the individual patient. However, as responsible members of society, physicians will probably want to consider efficiency in selecting medical care interventions more in the future than they have in the past. They will be torn between the decision to offer something extra to each patient without regard to cost and the decision to balance the effectiveress of an intervention with its cost in order to use society's (or the hospital's or the HMO's) resources most efficiently.

Morreim (85) characterizes this as a "moral challenge." Issues about allocation, such as the percent of GNP that is spent on health care, have seemed far removed from decision-making about individual patients. However, these decisions are now beginning to have an impact on decisions about individual patients. Thus, decisions about individual patients may be based on societal good rather than potential benefit for the individual patient. This is not consistent with physicians' training or patients' expectations, and will casue conflict, tension, and perhaps even re-definition of the physician's responsibility.

VIII. POLICY IMPLICATIONS

The available information about the clinical economics of nutrition support services and antibiotic medications provides some insight into the economic ramifications of the use of these two medical care interventions. Unfortunately, little specific information is available about the use of these two interventions for critically and terminally ill elderly patients. Moreover, there are methodologic weaknesses with many of the available studies, and data are not available about the economic implications that discriminate among the several possible points of view.

Investigators interested in resources used by critically and terminally ill patients have used a variety of definitions to identify the appropriate patient populations. While no one definition has been widely used or well accepted, several investigators have used charges or Medicare payments to identify high cost patients, and the relationship between high cost and critical illness has been established clearly. Other investigators have established that patients who die consume a large portion of third party payments. Nevertheless, the time frame for these analyses has varied and the studies have generally been conducted retrospectively. Therefore, no definition of terminal illness is available that may be applied prospectively. Assessing the economic ramifications of the use of particular interventions can only be conducted when it is possible to define clearly the patient population of interest. Once a definition is available, prospective randomized trials of medical interventions may be conducted to evaluate economic impacts. This first step is necessary to facilitate studies that are valuable for establishing societal, third party payer and institutional policies regarding the use of these services.

Investigations of the economic implications of nutrition support services and antibiotic medications generally have suffered from these and other methodologic weaknesses. For example, charges rather than true costs usually have been included in these analyses. Many studies have also been limited to resources consumed for delivering nutrition solutions and equipment, or for the antibiotic medications alone. Other real costs, such as those for preparing nutrition support solutions have rarely been included in the economic studies. Total cost information is important to consider as third party payers, including Medicare, adjust payment rates to more closely reflect the cost of delivering services.

Side-effects of nutrition support services and antibiotic medications are also important to consider, but costs for these events have rarely been included in economic assessments. For example, catheter-related infections or embolic events may result from receiving TPN. Different diagnostic and therapeutic interventions may be used to monitor and treat these adverse events. However, the resources consumed for these extra services have rarely be evaluated.

Another aspect of antibiotics and nutritional supplements that has not been included in the economic evaluations is that of adverse events avoided. For example, prophylactic use of antibiotic medications for surgical patients may prevent wound infections. Expenses are obviously incurred for the prophylactic antibiotic medications. However, these expenses may be small relative to the expenses that would be generated in diagnosing, treating and monitoring patients who develop wound infections. This category of costs is important to consider, for example, in a cost-effectiveness or cost-benefit study of the costs generated per wound infection prevented. In this sense, a patient who becomes critically ill because of a surgical complication may have been less expensive to treat if the complication had been prevented with an intervention such as prophylactic antibiotics or preoperative nutrition. For insurers and institutions, results of studies that incorporate these factors may be useful in developing policies that encourage increased use of specific prophylactic services, based on the lower expected incidence of costly adverse events.

Another weakness of the available literature is that investigators have concentrated on the use of nutrition support services and antibiotic medications for hospitalized patients; few investigators have conducted economic evaluations of the services used by nursing home patients. This component of the patient population should be considered; approximately 1 million elderly individuals are in nursing homes (70) and the overall nursing home patient population is predicted to increase as fixed-price payment programs and their inherent incentives to discharge patients from hospitals become more prevalant. Investigators have not focused on the use of antibiotic or nutrition support services by elderly patients. While individuals 65 years of age and over make-up 11 percent of the population, they account for over 30 percent of direct medical expenditures (12). Clinical economic studies should be focused on this segment of the population.

Third party payers may implement policies designed to minimize payments for nutrition support services and antibiotic medications. However, such policies may in fact increase the economic burden on patients, providers or society. For example, an insurer may make parenteral antibiotic therapy available on an outpatient basis, but insurer payments may be lower (and the patient would be responsible for copayment) for such a program than for inpatient care (hospital costs will also be lower and important to consider under fixed payment). Patients may be likely to incur greater expenses, including out-of-pocket expenses for direct nonmedical factors such as transportation to a hospital. Under such circumstances, patients are likely to resist outpatient care. Few data are available about these types of trade-offs. Nevertheless, they are important to consider in establishing payment programs and in estimating savings (to the insurer) that will accrue from the new program.

Methodologic approaches are available to address each of these issues. For example, Eisenberg and colleagues are conducting an economic evaluation as part of a VA cooperative study of preoperative nutrition support services delivered to nutritionally deficient surgical patients. They are assessing the actual hospital costs for acquiring, preparing and delivering nutrition support services. Costs for diagnostic and monitoring services, and consultations are also being included. Eisenberg et al are also assessing the cost of adverse postoperative events avoided, including extended length of stay and complications. Questionnaires and patient interviews are being used to determine patients' out-of-pocket and indirect expenses. The results of this study will include costs from patients', the hospitals' and the payer's (government) point of view.

Results of these types of studies will provide valuable information to policy-makers concerned with the economic impact of the use of specific heatlh care interventions. However, less tangible factors, including equity of resource distribution and ethical issues regarding withholding services, must also be considered by policy-makers. In an economic analysis that uses the human capital approach, elderly patients' lives would be devalued, thus biasing against interventions that prolong or save these patients' lives. As a society, however, it may be desirable to allocate resources to this group of patients. Such decisions, based on intangible factors, are difficult to define explicitly. Nevertheless, policies must be formulated that reflect these decisions.

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